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NEWS
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                  Federal Research in Progress (FEDRIP) now available
                  New e-mail delivery for search results now available
NEWS
          Jun 03
NEWS 10
          Jun 10
                  MEDLINE Reload
                  PCTFULL has been reloaded
NEWS 11
          Jun 10
          Jul 02
NEWS 12
                  FOREGE no longer contains STANDARDS file segment
NEWS 13
          Jul 22
                  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
          Jul 29
                  Enhanced polymer searching in REGISTRY
NEWS 14
                  NETFIRST to be removed from STN
NEWS 15
          Jul 30
                  CANCERLIT reload
NEWS 16
          Aug 08
NEWS 17
          Aug 08
                  PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18
          Aug 08
                  NTIS has been reloaded and enhanced
NEWS 19
          Aug 19
                  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
NEWS 20
          Aug 19
                  IFIPAT, IFICDB, and IFIUDB have been reloaded
          Aug 19
                  The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 21
NEWS 22
          Aug 26
                  Sequence searching in REGISTRY enhanced
NEWS 23
          Sep 03
                  JAPIO has been reloaded and enhanced
NEWS 24
          Sep 16
                  Experimental properties added to the REGISTRY file
NEWS 25
          Sep 16
                  CA Section Thesaurus available in CAPLUS and CA
NEWS 26
                  CASREACT Enriched with Reactions from 1907 to 1985
          Oct 01
NEWS 27
                  EVENTLINE has been reloaded
          Oct 21
NEWS 28
          Oct 24
                  BEILSTEIN adds new search fields
NEWS 29
          Oct 24
                  Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30
          Oct 25
                  MEDLINE SDI run of October 8, 2002
NEWS 31
          Nov 18
                  DKILIT has been renamed APOLLIT
NEWS 32
                  More calculated properties added to REGISTRY
          Nov 25
NEWS 33
          Dec 02
                  TIBKAT will be removed from STN
NEWS 34
         Dec 04
                  CSA files on STN
                  PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 35
          Dec 17
NEWS 36
          Dec 17
                  TOXCENTER enhanced with additional content
                  Adis Clinical Trials Insight now available on STN
NEWS 37
          Dec 17
                  ISMEC no longer available
NEWS 38
          Dec 30
                  Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 39
          Jan 13
                  NUTRACEUT offering one free connect hour in February 2003
NEWS 40
          Jan 21
NEWS 41
          Jan 21
                  PHARMAML offering one free connect hour in February 2003
NEWS 42
                  Simultaneous left and right truncation added to COMPENDEX,
          Jan 29
                  ENERGY, INSPEC
               January 6 CURRENT WINDOWS VERSION IS V6.01a,
NEWS EXPRESS
               CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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               STN Operating Hours Plus Help Desk Availability
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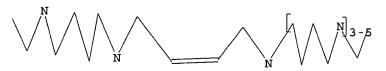
Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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SAMPLE SCREEN SEARCH COMPLETED - 96 TO ITERATE

100.0% PROCESSED 96 ITERATIONS

PERATIONS 1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 1333 TO 2507 PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 16:18:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 2348 TO ITERATE

100.0% PROCESSED 2348 ITERATIONS 8 ANSWERS

SEARCH TIME: 00.00.01

L3 8 SEA SSS FUL L1

=> fil caplus

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=> s 13

L4 6 L3

=> d l4 1-6 abs ibib hitstr

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS
AB Polyamine or polyamine analog-amino acid conjugates
(M)-N(E)-(B-A-B-NH)4-E
or (M)-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [M is an amino acid; A is a bond,
(cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; B is a bond, alkyl,
or alkenyl; E is H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl);
including salts or stereoisomers, were prepd. for use as antiviral
agents.

including salts or stereoisomers, were prepd. for use as antivital
agents.

An example is the polyamine glutamine conjugate SL-11165
[NH2CH(CH2CH2CONN2)CON(Et)(CH2CH2CH2CH2NH)4Et.bul.5HCl]. Thus,
(E)-btnNi(CH2)4NHCH2CH:CHC2NH(CH2)4NHEt was prepd. by a multi-step
sequence starting from 4-bromobutamenitrile, N(CH2CH2CH101)ethanamine, and (E)-2-butnen-1, 4-diol.

ACCLESSION NUMBER: 2002:88472 CAPLUS
DOCUMENT NUMBER: 137:384565
TITLE: Preparation of polyamine or polyamine analog-amino
acid conjugates as antiviral agents
Flydman, Benjamin: Marton, Laurence J.; Valasinas,
Aldonia L.; Reddy, Venodhar K.; Gutierrez, Jesus A.
SII Biomedical Corporation, USA; Eli Lilly & Company
DOCUMENT TYPE: PATENT
LANGUAGE: PATENT ACC. NUM. COUNT: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

Double bond geometry as shown.

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A

PAGE 1-B

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

●10 HCl

PAGE 1-B

304863-19-2P 304863-21-6P 304911-07-7P, SL
11144
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of polyamine or polyamine analog-amino acid conjugates as antiviral agents)
304863-19-2 CAPLUS
Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethyl-phenyl)sulfonyl]-5,10,15,20-tetrakis[(2,4,6-trimethyl-n-1

Double bond geometry as shown.

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

304863-21-6 CAPLUS Benzenesulfonamide, N,N'-(22)-2-butene-1,4-diylbis(2,4,6-trimethyl-N-[5,10,15,20-tetrakis((2,4,6-trimethylphenyl)sulfonyl)-5,10,15,20-tetraazadocos-1-yl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-B

PAGE 1-A

ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS Conjugates of polyamines analogs conjugated to at least one amino acid of formula M-N(E)-(B-A-B-NH) 4-E or M-N(E)-(B-A-B-NH) 3-B-A-B-N(M)-E [wherein

formula M-N(E)-(B-A-B-NH)4-E or M-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [wherein M

* independently an amino acid, esp. glutamine, asparagine, lysine, ornithine, arginine, histidine, or citrulline: A = independently a bond, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; B = independently a bond, alkyl, or alkenyl; E = independently H, (cyclo)alkyl, (cyclo)alkyl, or cycloaryl; and salts or stereoisomers thereof]

were tested and claimed for pharmaceutical use as anticancer agents. For example, the polyamine glutamine conjugate SL-11165 [NN2CH(CHZCHZCHONE)2CN)(E) (CHZCHZCHZCHNE)(CHZCHZCHZCH)) (ELDL-SHCL) = Shcl) exhibited ID50 values of >31.65, 4.1, and >31.25 against the DuPro, PC-3, and LnCap prostate cancer cell lines, resp. In addn., conformationally restricted polyamine analogs were prepd. Thus, (E)-ELNN (CHZ) 4NHCHZCH:CHCNENN (CHZ) 4NH E twas prepd. in a multi-step sequence starting from 4-bromobusenentrile,
N-mesitylethanamine, and (E)-2-butene-1,4-diol.
ACCESSION NUMBER: 2002:368258 CAPLUS
DOCUMENT NUMBER: 2002:368258 CAPLUS
DOCUMENT NUMBER: 136:386292
TITLE: Preparation of conformationally restricted polyamine analogs and use of polyamine amino acid conjugates as

136:386292
Preparation of conformationally restricted polyamine analogs and use of polyamine amino acid conjugates as anticancer agents
Frydman, Benjamin: Marton, Laurence J.; Valasinas, Aldonia L.; Reddy, Venodhar K.
Slil Biomedical Corporation, USA
PCT Int. Appl., 74 pp.
CODEN: PIXXD2
Patent
English
2 INVENTOR (S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2002038105 A2 20020516 WO 2001-US43595 20011108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, IK, LR, LS, LT, IJI, LV, MA, MD, MG, MK, ND, WK, MK, MZ, NZ, NO, MZ, OM, PH, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, VU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, M, RN, LP, TS, TR, BF, AU 2002035126 A5 20020521 AU 2002-235126 20011108

PRIORITY APPIN. INFO: US 2000-245868 W 2001-US43585 W 2001108

OTHER SOURCE(S): MARPAT 136:38625

T 304853-12-69, Benzenesulfonamide, N,N'-(22)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethyl-N APPLICATION NO. PATENT NO. KIND DATE DATE

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

304911-07-7 CAPLUS 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-B

ANSMER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) of polyamine amino acid conjugates as anticancer agents) 304863-19-2 CAPLUS Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[{2,4,6-trimethylphenyl}sulfonyl]-5,10,15,20-tetrakis[2,4,6-trimethylphenyl]sulfonyl]-5,10,10,15,20-tetrakis[2,4,6-trimethylphenyl]sulfonyl]-5,10,15,20-tetrakis[2,4,6-trimethylphenyl]sulfonyl]-5,10,10,15,20-tetrakis[2,4,6-trimethylphenyl]sulfonyl]-5,10,15,20-tetrakis[2

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

304863-21-6 CAPLUS
Benzenesulfonamide, N,N'-(22)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[[2,4,6-trimethylphenyl]sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

304911-07-7 CAPLUS 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-B

304911-08-6P, St 11150
RL: SPN (Synthetic preparation); PREP (Preparation)
(polyamine; prepn. of conformationally restricted polyamines and use

PAGE 1-B

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
polyamine amino acid conjugates as anticancer agents)
RN 304911-08-8 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine,
N,N'-diethyl-, decahydrochloride, (222)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-B

ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

AB The pre-emergent spore stages of Encephalitozoon cuniculi were evaluated for polyamine uptake and interconversion. The possible effects of SL-11150 en polyamine metab. Were also atudied. Enc. cuniculi was maintained on RK-13 cells, which were grown to 80% confluency in Corning T-26 or Falcon T-75 flasks and infected with 5 x 105 spores. Enc. cuniculi assimilated and interconverted polyamines; spermidine was taken up far more readily than spermine. A large proportion of the metabolites were excreted as in mammalian cells. The major effects of polyamine analogs on cells include competition for uptake through polyamine transporters, pregulation of spermidine/spermine N1-acetyltransferase, and excretion of polyamines, leading to redn. of polyamine content. The inhibition of metabolite prodn. and excretion by a low concn. of S1-11158 suggested that this polyamine analog targets, in part, polyamine interconversion in this perasite.

ACCESSION NUMBER: 2002:277765 CAPLUS

TITLE: SL-11158, a synthetic oligoamine, inhibits polyamine metabolism of Encephalitozoon cuniculi

AUTHOR(S): Bacchi, Cyrus J.; Orozoo, Daniel; Weiss, Louis M.; Frydman, Benjamin; Valasinasa, Aldonia; Yarlett,

Nigel;

RIFYCMBAN, Benjamin; Valasinas, Aldonia; Yarlett,

Nigel;

Marton, Laurence J.; Wittner, Murray
Haskins Laboratories, Pace University, New York, NY,
10038, USA
SOURCE: JOURNAL MICROSPHY
CODEN: JAMELD; ISSN: 1066-5234
CODEN: JAMELD; ISSN: 1066-5234
CODEN: JAMELD; ISSN: 1066-5234
COURNITYPE: Journal
LANGUAGE: English
IT 412351-17-8, SL-11158
RI: BSU (Biological study, unclassified); BIOL (Biological study)
(synthetic oligoamine SL-11158 inhibits polyamine metab. of
Encephalitozoon cuniculi)
RN 412351-17-8 CAPIUS
CN 5,10,15,20,25,30-Hexaaza-17-tetratriacontene-1,34-diamine, N,N'-diethyl-,
(17E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-B

REFERENCE COUNT: THIS

12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) L4

412351-16-7, SL 11157 412351-17-8, SL 11158
412351-20-3, SL 11172
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)
412351-16-7 CAPLUS

412331-16-7 CAPLUS 5,10,15,20,25,30-Hexaaza-17-tetratriacontene-1,34-diamine, N,N'-diethyl-, (172)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

/(CH2)4 (CH2)4

412351-17-8 CAPLUS 5,10,15,20,25,30-Hexasza-17-tetratriacontene-1,34-diamine, N,N'-diethyl-, (178)- (9CI) (CA INDEX NAME)

_ (CH₂) 4

PAGE 1-B

(CH2) 4 NHEt

412351-20-3 CAPLUS 5,10,15,20,25,30,35,40,45,50-Decaaza-27-tetrapentacontene-1,54-diamine, N,N'-diethyl-, (278)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS Microsporidia are ewharyotic obligate intracellular protists that are emerging pathogens in immunocompromised hosts, such as patients with AIDS or patients who have undergone organ transplantation. We have demonstrated in vitro and in vivo that synthetic polyamine analogs are effective antimicrosporidial agents with a broad therspeutic window. CDB-knockout mice or nude mice infected with the microsporidian Encephalitozoon cuniculi were cured when they were treated with four different novel polyamine analogs at doses ranging from 1.25 to 5 mg/kg

of

body wt./day for a total of 10 days. Cured animals demonstrated no
evidence of parasitemia by either PCR or histol. staining of tissues 30
days after untreated control animals died.

ACCESSION NUMBER: 2002:30291 CAPIUS

DOCUMENT NUMBER: 136:318859

Novel synthetic polyamines are effective in the
treatment of experimental microsporidiosis, an
opportunistic ALDS-associated infection

AUTHOR(S): Bacchi, Cyrus J.: Weiss, Louis M.: Lane, Schenella;
Frydman, Benjamin: Valesinas, Aldonia: Reddy,
Venedhar: Sun, Jerry S.: Marton, Laurence J.: Khan,
Imitiaz A.: Moretto, Magali; Yarlett, Nigel; Wittner,
Murray

CORPORATE SOURCE:

SOURCE:

Imitiaz A.; Moretto, Magali; Yarlett, Nigel; Wittner, Murray
Haskins Laboratories and Departments of Biology and Chemistry, Pace University, New York, NY, 10038-1598, USA
Antimicrobial Agents and Chemotherapy (2002), 46(1), 55-61
CODEN: AMACCO; ISSN: 0066-4804
American Society for Microbiology
Journal
English
4

CODEN: AMACCQ; ISSN: 0066-4804

American Society for Microbiology

DOCUMENT TYPE: Journal
LANGUAGE: English

T 304911-07-7, SL 11144

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(SL 11144; novel synthetic polyamines are effective in treatment of exptl. microsportidosis, opportunistic AIDS-assocd. infection)

RN 304911-07-7 CAPLUS

CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine,

N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

●10 HC1

PAGE 1-B

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-B

PAGE 1-C

-- NHET

FORMAT

REFERENCE COUNT: THIS

THERE ARE 45 CITED REFERENCES AVAILABLE FOR RECORD. ALL CITATIONS AVAILABLE IN THE RE

```
ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS Novel conformationally restricted polyamines, such as E-NH-(B-A-B-NH) 4-E [A, E = bond, alkyl, alkenyl, alkynyl, cycloalkyl, cycloaryl, cycloalkenyl; B = bond, alkyl, alkenyl], were prepd. for pharmaceutical use as anticancer agents. Thus, (E)-EthH(CH2)*AHCH2CH:CH2NH(CH2)*ANNE was prepd. in a multistep sequence starting from mesityl chloride 4-bromobutanenitrile, N-mesitylethanamine, and (E)-2-butene-1,4-diol.
              prepd. polyamines were tested for antiproliferative activity against
human prostate cancer cell lines, such as PC3 and DUPRO.
ACCESSION NUMBER: 2000:790505 CAPLUS
DOCUMENT NUMBER: 133:350095
DOCUMENT NUMBER:
TITLE:
                                                                      133:350095
Preparation of conformationally restricted polyamine analogs as disease therapies
Frydman, Benjamin, Marton, Laurence J.; Reddy,
Venodhar K.; Valasinas, Aldonia; Blokhin, Andrei V.;
INVENTOR(S):
                                                                     Velicinar K., Velasinas, Aldonia,
Basu, Hirak S.
Slil Biomedical Corporation, USA
PCT Int. Appl., 135 pp.
CODEN: PIXXD2
Patent
PATENT ASSIGNEE(S):
DOCUMENT TYPE:
 LANGUAGE:
                                                                      English
 FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT NO.	KIND DATE	APPLICATION NO. DATE							
WO 2000066587	A2 20001109	WO 2000-US11591	20000427						
WO 2000066587	A3 20010125								
W: AE, AG,	AL, AM, AT, AU,	AZ, BA, BB, BG, BR, BY,	CA, CH, CN, CR,						
		EE, ES, FI, GB, GD, GE,							
		KG, KP, KR, KZ, LC, LK,							
		MW, MX, NO, NZ, PL, PT,							
		TR, TT, TZ, UA, UG, US,							
	AZ, BY, KG, KZ,								
		SL, SZ, TZ, UG, ZW, AT,	BE, CH, CY, DE,						
		IE, IT, LU, MC, NL, PT,							
		ML, MR, NE, SN, TD, TG							
		EP 2000-928583	20000427						
R: AT, BE,	CH, DE, DK, ES,	FR, GB, GR, IT, LI, LU,	NL. SE. MC. PT.						
	LT, LV, FI, RO		-,,,						
		BR 2000-10701	20000427						
		JP 2000-615617							
PRIORITY APPLN. INFO									
		WO 2000-US11591 W							
OTHER SOURCE(S):	MARPAT 133:	350095							
IT 304863-62-5P 304	911-08-8P, SL 11	150							
		effector, except advers	e); BSU						
(Biological	•	•							
study, unclassi	fied); SPN (Synt	netic preparation); THU	(Therapeutic use);						
		Preparation); USES (Uses							
		restricted polyamines as							

prostate cancer agents)
304863-62-5 CAPLUS
3,8,13,18,23,28,33,38,43,48-Decaazapentacont-25-en-1-ol,
decahydrochloride, (252)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-B

304911-08-8 CAPLUS 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (222)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

304863-19-2P 304863-21-6P 304911-07-7P, SL
11144
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of conformationally restricted polyamines as antiproliferative prostate cancer agents)
304863-19-2 CAPLUS
Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 2-A (CH₂) 4 (CH₂) 4

304863-21-6 CAPLUS
Benzenesulfonamide, N,N'-[22]-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-B

ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS
The invention relates to peptide conjugates in which cytocidal and
cytostatic agents, such as polyamine analogs or naphthoquinones, are
conjugated to a polypeptide recognized and cleaved by enzymes such as
prostate-specific antiqen (FSA) and cathepsin B. Methods of using these
conjugates in the treatment of prostate diseases are also provided.

Conjugates in the treatment of prostate diseases are also provided.

Thus,

C2[CH2NH(CH2)4NHEt]2.4HCl (SL-11103), 4-[[7-[4-(9acridinylaminolphenyl|heptyl|oxy]-1,2-naphthoquinone (SL-11064), and
morpholino-Ser-Lys-Leu-Gin-.beta.-Ala-.beta.-lapachone (SL-11147) were
prepd. and assayed for antitumor activity against human prostate cancer
cell lines, such as PC-3 and DUBRO.

ACCESSION NUMBER:
DOCUMENT NUMBER:
133:350515

TITLE:
Preparation of novel polyamine analog conjugates and
quinone conjugates as therapies for cancers and
prostate diseases
INVENTOR(S):
FYDMAN, Benjamin; Marton, Laurence J.
FYDENT ASSIGNEE(S):
SUIL Biomedical Corporation, USA
PCT Int. Appl., 194 pp.
CODEN: PIXXD2

DOCUMENT TYPE:
PATENT ASSIGNEE(S):
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:

PATENT	INFO	RMATI	ON:														
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W	0 200	00661	75	A	3	2001	0802										
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR
		Cυ,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	ΗU
		ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU
		LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE
		SG,	SI,	sĸ,	SL,	TJ,	TM,	TR,	TT,	TZ,	UΑ,	UG,	US,	UZ,	VN,	YU,	ZA
		ZW,	AM,	AZ,	BY,	KG,	ΚZ,	MD,	RU,	TJ,	TM						
	RW	: GH,	GM,	ΚE,	LS,	MW,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE
		DK,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF
							GW,										
E	P 117																
	R:	AT,						FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT
							RO										
	R 200																
	P 200																
PRIORI	TY AP	PLN.	INFO	.:					US 1	999-	1318	09P	P	1999	0430		
										2000-	US11	542	W	2000	0427		
OTHER	SOURC	E(S):			MAR	PAT	133:	3505	15								

OTH IT

R SOURCE(S): MARPAT 133:350515
304863-19-2P 304863-21-6F 304911-07-7P
30491-08-8P, SL 11150
RL: RCT (Reactant): SPN (Synthetic preparation): PREP (Preparation): RACT (Reactant or reagent)
(prepn. of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases)
304863-19-2 CAPLUS
Benzenesulfonamide, N,N'-(2E)-2-butene-1, 4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetrakis[0]

Double bond geometry as shown.

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

304911-07-7 CAPLUS 5,10,15,20,25,30,35,40-0ctaszatetratetracont-22-ene-1,44-diamine,N-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

●10 HCl

PAGE 1-B

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A

PAGE 1-B

 $\label{eq:capacity} 304863-21-6 \quad CAPLUS \\ \text{Benzenesulfonamide}, \quad N,N'-(22)-2-\text{butene-1}, 4-\text{diylbis}\{2,4,6-\text{trimethyl-N-5},10,15,20-\text{tetrakis}\{\{2,4,6-\text{trimethylphenyl}\}\text{ sulfonyl}\}-5,10,15,20-\text{tetrakis}\{2,4,6-\text{trimethylphenyl}\}\text{ sulfonyl}\}-5,10,15,20-\text{tetrakis}\{2,4,6-\text{trimethylphenyl}\}\text{ sulfonyl}\}-5,10,15,20-\text{tetrakis}\{2,4,6-\text{trimethylphenyl}\}\text{ sulfonyl}\}-5,10,15,20-\text{tetrakis}\{2,4,6-\text{trimethylphenyl}\}\text{ sulfonyl}\}-5,10,15,20-\text{tetrakis}\{2,4,6-\text{trimethylphenyl}\}\text{ sulfonyl}\}-5,10,15,20-\text{tetrakis}\{2,4,6-\text{trimethylphenyl}\}\text{ sulfonyl}\}-5,10,15,20-\text{tetrakis}\{2,4,6-\text{trimethylphenyl}\}\text{ sulfonyl}\}-5,10,15,20-\text{tetrakis}\{2,4,6-\text{trimethylphenyl}\}-5,10,15,10,15,10,15,10,15,10,15,10,15,10,15,10,1$

Double bond geometry as shown.

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

304911-07-7 CAPLUS 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

●10 HC1

PAGE 1-B

304911-08-8 CAPLUS 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (222)- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS Double bond geometry as shown.

PAGE 1-B

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STRUCTURE FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4 DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

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SAMPLE SEARCH INITIATED 16:24:54 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 13 TO ITERATE

100.0% PROCESSED 13 ITERATIONS 1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

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PROJECTED ITERATIONS: 476 44 TO

PROJECTED ANSWERS: 1 TO

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FULL SEARCH INITIATED 16:24:58 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 238 TO ITERATE

100.0% PROCESSED 238 ITERATIONS 28 ANSWERS

SEARCH TIME: 00.00.01

L7 28 SEA SSS FUL L5

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COST IN U.S. DOLLARS SINCE FILE TOTAL

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ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS
The invention is a series of novel and effective inhibitors of integrase, an essential in the life cycle of retroviruses. These compds. were designed to have a restricted conformation for the detn. of the integrase binding site and mechanism of inhibition. The integrase inhibitors of

the invention are effective in the submicromolar range, and thereby provide novel lead compds. for the development of anti-viral therapeutics.

ACCESSION NUMBER: 2002:31406 CAPLUS
DOCUMENT NUMBER: 136:7937
TITLE: Symmetric inhibitors of HIV integrase, mammalian topolsomerase and serineprotease
HAVENTOR(S): HAVENTOR(S): Themas Jefferson University, USA PCT Int. Appl., 42 pp.
CODEN: PIXXOZ
DOCUMENT TYPE: PCDEN: PIXXOZ
FAMELY ACC. NUM. COUNT: English
FAMELY ACC. NUM. COUNT: English
FAMELY INFORMATION:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2002002516 A2 20020110 W0 2001-US19923 20010622

W: CA, JP

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO: US 2000-215474P P 20000630

IT 387397-93-5P, RWH 23

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(sym. inhibitors of HIV integrase, mammalian topoisomerase and serineprotease)

RN 387397-93-5 CAPLUS

Benzenecarboximidamide, 4,4'-[(2,3-dihydroxy-1,4-butanediyl)diimino]bis-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{NH} \\ \text{H}_2\text{N-} \\ \\ \end{array} \\ \begin{array}{c} \text{OH} \\ \text{OH} \\ \\ \text{OH} \\ \\ \text{C} \\ \end{array} \\ \begin{array}{c} \text{NH} \\ \\ \text{C} \\ \\ \text{NH} \\ \end{array} \\ \begin{array}{c} \text{C} \\ \text{NH} \\ \\ \end{array} \\ \end{array}$$

L8 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

125880-82-2 CAPLUS

123000-62-2 CAPLUS Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)

NH- (CH2) 4

125880-83-3 CAPLUS Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis(3-nitro- (9CI)(CA INDEX NAME)

125880-84-4 CAPLUS Benzenecarboximidamide, 4,4'-{1,5-pentanediyldimino}bis[3-nitro- {9CI} (CA INDEX NAME)

(CH2)5

125880-86-6 CAPLUS
Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino-(9CI)(CA INDEX NAME)

-NH- (CH2) 4-NE

RN 125880-89-9 CAPLUS

ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS
A proposed model for the interaction of bisamidine analogs with the B-DNA receptor is established by structure-property relationship studies ved
from 3D-WHIM descriptor calcus. Three classes, each with relevant
information about structural relationships, were detd, by PCA and SIMCA
analyses for mol. conformations described by 3D-WHIM descriptors for a

of 29 bisamidines with antileishmaniasis and anti-PCP activities. Shape, distribution and dimension properties mostly govern the interaction of bisamidines with B-DNA through the minor groove AT rich regions.

ACCESSION NUMBER: 2000:664385 CAPLUS

DOCUMENT NUMBER: 133:344182

TITLE: 3D-WHIM pattern recognition study for bisamidines. A structure-property relationship study

AUTHOR(S): Menezes, Fabiano A. S.; Montanari, Carlos A.; Bruns, Roy E.

Roy E. Departamento de Quimica, Universidade Federal de CORPORATE SOURCE:

Gerais, Belo Horizonte, 31270-901, Brazil Journal of the Brazilian Chemical Society (2000), 11(4), 393-397 CODEN: JOCSET; ISSN: 0103-5053 Sociedade Brasileira de Quimica SOURCE:

CODEN: JOCSET: ISSN: 0103-5053

PUBLISHER: Sociedade Brasileira de Quimica

DOCUMENT TYPE: Journal

LANGUAGE: English

1 124076-63-7 125880-81-1 125880-82-2

125880-83-3 125880-84-4 125880-86-6

125880-89-9

RI: BAC (Biological activity or effector, except adverse); BSU

logical study, unclassified); BIOL (Biological study) (3D-WHIM pattern recognition and structure-activity relationship study for bisamidines) 124076-63-7 CAPLUS

Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA NAME)

125880-81-1 CAPLUS

Benzenecarboximidamide, 4,4'-(1,3-propanediyldimino)bis- (9CI) (CA INDEX NAME)

ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued) Benzenecarboximidamide, 4,4'-(1,2-ethanediyldimino)bis(3-amino-(9CI)(CA INDEX NAME)

REFERENCE COUNT: THIS

FORMAT

THERE ARE 31 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE

```
ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS Arom. dicationic drugs have a broad spectrum of activity against
                     and fungal pathogens including Pneumocystis carinii, Leishmania mexicana amazonensis, Cryptosporidium parvum, and Cryptococcus neoformans. Pentamidine serves as the exemplar for an extensive collection of newly synthesized related compds., which have reduced toxicity and a wider
                   synthesized related compds., which have reduced toxicity and a wider e of target organisms. Assays of pentamidine and related compds. have depended on HPLC-tandem mass spectrometry (HPLC-TMS) for the quantitation and identification of drug and metabolites. Immunoassays for pentamidine would have many advantages over the MPLC methods including relative simplicity of assay format and required equipment, convenience in sample prepn. and redn. in time and cost of assays. In this report the authors describe a simple ELISA based immunoassay for pentamidine and pentamidine-like drugs with requisite sensitivity and specificity for use as a clin. assay (ECSO value of about 50 nanomolar). Immunogen was synthesized by coupling the hapten aminopentamidine to ovalbumin (chem. modified to provide an optimal no. of -SH groups) using sulfo-MBS. Maleic-enhydride activated ELISA plates were covalently sensitized using the amino-pentamidine hapten and used in an inhibitory ELISA assay format whereby the ability of analyte to suppress antibody binding to sensitized plate was measured. The assay detects primarily the phenolic amidine of pentamidine when in a para position and hence can also detect curally
structure11y
related derivs. of pentamidine of potential interest as new therapeutic
agents.

ACCESSION NUMBER: 2000:204083 CAPLUS
                                                                                                            2000:204083 CAPLUS
133:114510
133:114510
Immunoassays for pentamidine and related compounds:
development of a facile inhibitory ELISA suitable for
clinical use
Reismer, Howard M.: Gray, Danny R.: Jones, Susan K.:
Rose, Beate G.: Tidwell, Richard R.
Department of Pathology and Laboratory Medicine,
School of Medicine, University of North Carolina at
Chapel Hill, Chapel Hill, NC, 27599-7525, USA
Journal of Clinical Laboratory Analysis (2000),
 DOCUMENT NUMBER
 TITLE:
AUTHOR (S):
CORPORATE SOURCE:
 SOURCE .
                                                                                                             /3-82
CODEN: JCANEM; ISSN: 0887-8013
Wiley-Liss, Inc.
Journal
 PUBLISHER:
DOCUMENT TYPE:
LANGUAGE:
IT 124076-63-7
RI: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therape
                ological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses) (immunoassays for pentamidine and related compds.) 124076-63-7 CAPLUS
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Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA

ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS

NAME)

RRINCOCHR2NHZC(:NG1)NHG2 {I; 1 of G1,G2 = H and the other = H, OH, alkyl, alkoxy, etc.; R = (un)substituted alkyl, cycloalkyl, aryl; R1 = H or alkyl; R2 = (un)substituted Ph or -pyridyl; Z = (3-hydroxy)

a.kyl: RZ = (un)substituted Ph or "pyridyl: Z = (3-hydroxy)
1,4-phenylene]
, were prepd. Thus, 3,4-(MeO)(PhCH2O)C6H3CHO, 4-(H2N)C6H4C(:NH)NH2, and
PhCH2NC were condensed to give, after acidification, title compd. II.HCl.
Data for biol. activity of I were given.
ACCESSION NUMBER: 1999:375282 CAPLUS
DOCUMENT NUMBER: 131:4656
TITLE: Preparation of N-(4-amidinophenyl)phenylglycineamides

131:44656
Preparation of N-(4-amidinophenyl)phenylglycineamides as factor VIIa/tissue factor inhibitors
Grobke, Katrin; Ji, Yu-hua; Wallbaum, Sabine; Weber,

INVENTOR(S):

LUCZ
F. Hoffmann-La Roche A.-G., Switz.
EUr. Pat. Appl., 46 pp.
CODEN: EPXXDW
Patent PATENT ASSIGNÉE(S): SOURCE:

DOCUMENT TYPE:

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PA'	FENT !	NO.		KI	ΝD	DATE			AP	PLIC	ATIC	N NO	٥.	DATE			
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		ΙE,	SI,	LT,	LV,	FI,	RO										
US	6140	353		A		2000	1031		US	199	8-20	4373	3	1998	1202		
ZA	9811	077		A		1999	0604		ZA	199	8-11	077		1998	1203		
NO	9805	646		A		1999	0607		NO	199	8-5 6	46		1998	1203		
ΑU	9895	210		A.	1	1999	0624		ΑU	199	8-95	210		1998	1203		
ΑU	7397	69		В2	2	2001	1018										
CN	1224	714		А		1999	0804		CN	199	8-12	6979	•	1998	1204		
JP	1124	6507		A.	2	1999	0914		JP	199	8-34	15875	5	1998	1204		
JP	3236	267		В:	2	2001	1210										
BR	9805	320		A		2000	0411		BR	199	8-53	120		1998	1204		

ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

REFERENCE COUNT: THIS

THERE ARE 38 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L8 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)
PRIORITY APPLN. INFO.: EP 1997-121285 A 19991110
EP 1998-121374 A 19991110 OTHER SOURCE(S): MARPAT 131:44656 227021-09-1P RL: BAC (Biological activity or effector, except adverse); BSU ogical study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) [Prepn. of N-(4-amidinophenyl)phenylglycineamides as factor VIIa/tissue /tissue
 factor inhibitors)
227021-08-1 CAPLUS
Benzeneacetamide, N-[4-(aminoiminomethyl)phenyl]-.alpha.-([4(aminoiminomethyl)phenyl]amino]-3-methoxy-4-(phenylmethoxy)-, acetate
(9CI) (CA INDEX NAME) CM 1 CRN 227021-07-0 CMF C30 H30 N6 O3

СМ 2

- CH 2

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT .

Twenty analogs of pentamidine (including I), 7 primary metabolites of pentamidine, and 30 dicationic substituted bisbenzimidazoles were

pentamidine, and 30 dicationic substitutes against Candida albicans screened for their inhibitory and fungicidal activities against Candida albicans and Cryptococcus neoformans. A majority of the compds. had MICs at which 80% of the strains were inhibited (MIC80s) comparable to those of amphotericin B and fluconazole. Unlike fluconazole, many of these compds., such as II and III, were found to have potent fungicidal activity. The most potent compd. against C. albicans had an MIC80 of .ltoreq.0.09 .mu.g/mL, and the most potent compd. against C. neoformans had an MIC80 of 0.19 .mu.g/mL. Selected compds., such as IV, were also found to be active against Aspergillus fumigatus, Fusarium solani, Candida

species other than C. albicans, and fluconazole-resistant strains of C. albicans and C. neoformans. It is clear from the data presented here

albicans and C. neoformans. It is clear from the data presented here that further studies on the structure-activity relationships, mechanisms of action and toxicities, and in vivo efficacies of these compds. are warranted to det. their clin. potential.

ACCESSION NUMBER: 1998:664985 CAPLUS

DOCUMENT NUMBER: 130:22732

TITLE: Structure-in vitro activity relationships of pentamidine analogs and dication-substituted bis-benzimidazoles as new antifungal agents bel Poeta, Maurizior Schell, Wiley A.: Dykstra, Christine C.: Jones, Susan; Tidwell, Richard R.: Czarny, Agnieszka; Bajic, Miroalav: Bajic, Marina: Kumar, Arvind; Boykin, David; Perfect, John R. Department of Medicine, Division of Infectious Diseases and International Health, Duke University Medical Center, Durham, Nc. 27710, USA

Antimicrobial Agents and Chemotherapy (1998), 42(10), 2499-2502

CODEN: AMARCO: ISSN: 0066-4804

CODEN: AMACCQ; ISSN: 0066-4804 American Society for Microbiology

PUBLISHER: AMMCION DOCUMENT TYPE: Journal LANGUAGE: English IT 124076-63-7 125880-81-1 125880-83-3

125880-85-5 RL: BAC (Biological activity or effector, except adverse); BSU (Biological

logical
study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(structure-in vitro activity relationships of pentamidine analogs and
dication-substituted bis-benzimidazoles as new antifungal agents)
124076-63-7 CAPLUS
Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA

NAME)

ANSWER 6 OF 19 CAPLUS COPYRIGHT 2003 ACS

Arom. dicationic compds., such as pentamidine, have potent antimicrobial activities. Clin. use of these compds. has been restricted, however, by their toxicity and limited oral activity. A novel approach, using amidoxime derivs. as prodrugs, has recently been proposed to overcome these limitations. Although results were presented for amidoxime derivs. of only one diamidine, pentamidine, the authors in the original proposal claimed that amidoxime derivs. would work as effective prodrugs for all pharmacol. active diamidines. Nine novel amidoxime derivs. were synthesized and tested in the present study for activity against Pneumocystis carinii in corticosteroid-suppressed rats. Only three of

nine compds. had significant oral anti-Pneumocystis activity. The bisbenzamidoxime derivs. of three direct pentamidine analogs had

Disberzamidoxime derivs. of three direct pentamidine shalogs had excellent oral and i.v. activities and reduced acute host toxicity. These compds are not likely candidates for future drug development, however, because they have chronic toxic effects and the active amidine compds. have multiple sites susceptible to oxidative metab., which complicates their pharmacol. and toxicol. Novel diamidoximes from three other structural classes, contg. different groups linking the cationic moieties, lacked significant oral or i.v. anti-Pneumocystis activity, even though the corresponding diamidines were very active i.v. Both active and inactive amidoximes were readily metabolized to the corresponding amidines by cell-free liver homogenates. Thus, the amidoxime prodrug approach may provide a strategy to exploit the potent antimicrobial and other pharmacol. activities of selected, but certainly not all, arom. diamidines.

ACCESSION NUMBER: 198:189774 CAPLUS
DOCUMENT NUMBER: 128:303628
TITLE: ARTIPREUMOCYSTIS activities of aromatic diamidoxime prodrugs

1988:189774 CAPLUS
128:303628
Anti-Pheumocystis activities of aromatic diamidoxime prodrugs
Hall, James Edwin, Kerrigan, John E.; Ramachandran, Kishore; Bender, Brendan C.; Stanko, Jason P.; Jones, Susan K.; Patrick, Donald A.; Tidwell, Richard R. Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, Nc, 27599, USA Antimicrobial Agents and Chemotherapy (1998), 42(3), 666-674
CODEN: AMACCQ; ISSN: 0066-4804
American Society for Microbiology
Journal
English AUTHOR (5):

CORPORATE SOURCE: SOURCE:

PUBLISHER: DOCUMENT TYPE: LANGUAGE:

206532-33-4P

IT 206532-33-4P
RL: BAC (Biological activity or effector, except adverse); BPR
(Biological
process); BSU (Biological study, unclassified); PRP (Properties); SPN
(Synthetic preparation); PRO (Therapeutic use); BIOL (Biological study);
PREP (Preparation); PROC (Process); USES (Uses)
(anti-Pneumocystis activities of arom. diamidoxime prodrugs in

to structure and metab. and toxicity)
206532-33-4 CAPLUS
Propanediamide, N,N'-bis[4-{(hydroxyamino)iminomethyl]phenyl]- (9CI) (CA
INDEX NAME)

L8 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

125880-81-1 CAPLUS
Benzenecarboximidamide, 4,4'-(1,3-propanediyldimino)bis- (9CI) (CA NAMES

125880-83-3 CAPLUS Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

125880-85-5 CAPLUS
Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis{3-amino-(9CI)(CA INDEX NAME)

REFERENCE COUNT: THERE ARE 41 CITED REFERENCES AVAILABLE FOR RECORD. ALL CITATIONS AVAILABLE IN THE RE

ANSWER 6 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

IT 206532-34-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

Study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(anti-Pneumocystis activities of arom. diamidoxime prodrugs in relation

to structure and metab. and toxicity)
205532-34-5 CAPLUS
Propanediamide, N,N'-bis[4-(aminoiminomethyl)phenyl]- (9CI) (CA INDEX NAME)

ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS Results are presented for a QSAR anal. of bisamidines, using a similarity index as descriptor. The method allows for differences in conformation of

bisamidines at the receptor site to be taken into consideration. In particular, it has been suggested by others that pentamidine binds in the minor groove of DNA in a so-called isohelical conformation, and the authors QSAR supports this suggestion. The mol. similarity index for comparison of mols. can be used as a parameter for correlating and hence rationalizing the activity as well as suggesting the design of bioactive mols. The studied compds had been evaluated for potency against Leishmania mexicana amazonensis, and this potency was used as a dependent variable in a series of QSAR analyses. For the calcn. of similarity indexes, each analog was in turn superimposed on a chosen lead compd. in

ref. conformation, either extended or isohelical, maximizing overlap and hence similarity by flexible fitting.

ACCESSION NUMBER: 1996:162810 CAPLUS

DOCUMENT NUMBER: 124:277974

TITLE:

AUTHOR(S):

124:277974

Determination of receptor-bound drug conformations by QSAR using flexible fitting to derive a molecular similarity index

Montanari, C. A.; Tute, M. S.; Beezer, A. E.;

Mitchell, J. C.

Chem. Lab., Univ. Kent, Canterbury, Kent, C72 7NH, UK
Journal of Computer-Aided Molecular Design (1996), 10(11. 67-73 CORPORATE SOURCE:

10(1), 67-73 CODEN: JCADEQ; ISSN: 0920-654X

PUBLISHER:

DOCUMENT TYPE: LANGUAGE: IT 124076-63-JOURNAL LAGGE: English 124076-63-7 125880-81-1 125880-82-2 125880-83-3 125880-84-4 125880-86-6 125880-87-7 125880-89-9 RL: BAC (Biologica)

RL: BAC (Biological activity or effector, except adverse); BSU

RI: BAC (Bloingical activity of the field of the field of the field) given the field; BIOL (Biological study); USES (Uses) (Getn. of receptor-bound drug conformations on DNA by QSAR using flexible fitting to derive a mol. similarity index using bisamidines

Leishmania inhibitors)
124076-63-7 CAPLUS
Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX

NAME)

125880-81-1 CAPLUS
Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA INDEX NAME)

ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino- (9CI)(CA INDEX NAME)

RN CN

Benzenedarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI)(CA INDEX NAME)

ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

125880-82-2 CAPLUS

Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX

125880-83-3 CAPLUS

Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis(3-nitro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{NO2} & \text{NH- (CH_2)} \text{ } 3-\text{NH- } \\ & \text{H_2N-C} & \\ & \text{NH} & \text{NH} \end{array}$$

125880-84-4 CAPLUS
Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME) RN CN

125880-86-6 CAPLUS Benzenecarboximidamide, 4,4'-{1,4-butanediyldiimino}bis[3-amino- (9CI) (CA INDEX NAME)

ANSWER 8 OF 19 CAPLUS COPYRIGHT 2003 ACS
The in vitro culture system is described in which Trypanosoma brucei
rhodesiense (LOUTat.) was grown with the human feed layer cell HL-60.
The use of this system in detg. the 50% growth Inhibitory Concn. (IC50)

of unknown compds. for both the trypanosomes and the host cell was demonstrated. The data shows that several analogs of pentamidine have significantly reduced host cell toxicity but maintain or have increased trypanocidal activity. The value of the trypanosome/HL-60 in vitro culture system as a rapid primary in vitro drug screen is discussed. Based upon the ability of this primary screen to predict potential drug efficacy, several analogs screened in vitro were then tested in vivo.

results of the in vivo tests confirmed the ability of the in vitro screen to predict drug efficacy, and also suggests that better analogs of pentamidine (less host toxicity and greater trypanocidal activity) can be obtained to treat human trypanosomiasis. SION NUMBER: 1996:138520 CAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER: 124:249761

The in vitro HL-60 cell - Trypanosoma brucei rhodesiense culture system: A rapid in vitro drug

AUTHOR(S): CORPORATE SOURCE:

rhodesiense culture system: A rapid in vitro drug screen Keku, T. O.; Seed, J. R.; Tidwell, R. R. Department of Medicine, University North Carolina, Chapel Hill, NC, USA Tropical Medicine and Parasitology (1995), 46(4), 258-62 SOURCE:

CODEN: TMPAEY: ISSN: 0177-2392

PUBLISHER: Thieme

DOCUMENT TYPE: LANGUAGE: English

124076-63-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES

(in vitro HL-60 cell-Trypanosoma brucei rhodesiense culture system for rapid in vitro trypanocidal drug screening) 124076-63-7 CAPLUS Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA

RN CN INDEX NAME.

L8 ANSMER 9 OF 19 CAPLUS COPYRIGHT 2003 ACS
AB A mol. mechanics and mol. dynamics approach has been used to examine the structure of the complex formed between pentamidine and the d(CGCGAATTCGCG)2 duplex. Similar energy calcus, have also been performed on complexes with closely related pentamidine analogs, using the complex with the parent drug as the starting point. The resulting structures of the drug-DNA complexes and their energetics have been examed, and are compared with the reported DNA binding affinities. These studies provide rationalizations for the differences in binding behavior of pentamidine analogs with differing linker chain lengths and arom. ring substitutions.

ACCESSION NUMBER: 1993:673590 CAPLUS
DOCUMENT NUMBER: 1993:673590 CAPLUS
DNA minor groove recognition properties of pentamidine
and its analogs: A molecular modeling extent. and its analogs: A molecular modeling study Greenidge, Paulette A.; Jenkins, Terence C.; Neidle, Stephen Cancer Res. Campaign Biomol. Struct. Unit, Inst. Cancer Res., Sutton/Surrey, SMZ SNG, UK Molecular Pharmacology (1993), 43(6), 982-8 CODEN: MOPMA3; ISSN: 0026-895X Journal English AUTHOR (S) CORPORATE SOURCE: CODEN: MOPMA3; ISSN: 0026-895X

DOCUMENT TYPE: Journal
LANGUAGE: English

IT 124076-63-7
RI: BIOL (Biological study)
(DNA minor groove recognition properties of, anti-Pneumocysis carinii
activity in relation to)
RN 124076-63-7 CAPJUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA NAME)

ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS
The error of omitting the supplementary material available paragraph has been cor. The error was not reflected in the abstr. or the index ACCESSION NUMBER: 1993:51883 CAPLUS DOCUMENT NUMBER: TITLE: 118:51883 118:51883
Structure and DNA binding activity of analogs of 1,5-bis(4-amidinophenoxy)pentane [pentamidine].
[Erratum to document cited in Call16(9):75694b]
Cory, Michael; Tidwell, Richard R.; Fairley, Terri P.
Div. Org. Chem., Burroughs Wellcome Co., Research
Triangle Park, NC, 27709, USA
Journal of Medicinal Chemiatry (1992), 35(25), 4767
CODEN: JMCMAR; ISSN: 0022-2623 AUTHOR (S): CORPORATE SOURCE: SOURCE: CODEN: JMCMAR; ISSN: 0022-2623

JMCHT TYPE: Journal

LAGE: English

124076-63-7 12580-81-1 125880-82-2

12580-83-3 12580-84-4 12580-05-5

125800-86-6 125800-87-7 125800-89-9

RL: BAC (Biological activity or effector, except adverse); BSU DOCUMENT TYPE: RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (DNA-binding activity of (Erratum))
RN 124076-63-7 CAPJUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA NAME I

125880-81-1 CAPLUS
Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA NAME

125880-82-2 CAPLUS Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)

ANSWER 10 OF 19 CAPLUS COPYRIGHT 2003 ACS
We have investigated the interactions of six analogs of pentamidine with
the N-mechyl-D-aspartate (NMDA) receptor complex. All six compds. were
effective NMDA receptor antagonists based upon their ability to inhibit
[3H]dizocilpine binding to rat brain membranes. IC50 values ranged from 2

to 18 .mu.M, and all compds. had Hill coeffs. in excess of 1 suggesting a non-competitive interaction with [3H]dizocilpine. All compds. also inhibited NMDA- and glycine-induced intracellular Ca2+ changes measured

inhibited NMDA- and glycine-induced intracellular Ca2+ changes measured in cultured rat forebrain neurons using the fluorescent indicator, fura-2. ICSO values in this assay ranged from 0.4 to 4.7 mu.M. Whereas pentamidine is directly toxic to cultured neurons, this was not a consistent finding with the pentamidine analogs tested, indicating that the toxic effects are not related to NMDA receptor antagonism. Finally, all of the agents tested were also effective in protecting neurons from NMDA-induced neurotoxicity. These data emphasize the possible utility of pentamidine-like drugs as neuroprotective agents and suggest that it is possible to generate compds. with a wider margin of safety than pentamidine itself.

ACCESSION NUMBER: 1993:160558 CAPLUS
DOCUMENT NUMBER: 118:160558
STUTILE: Studies on the effects of several pentamidine analogs on the NMDA receptor
AUTHOR(S): Reynolds, Ian J. Zeleski, Diane M.; Rothermund, Kristi D.; Hartnett, Karen A.; Tidwell, Richard; Aizenman, Elias Dep. Pharmacol., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA
SOURCE: DEPPET, ISSN: 0522-4106
DOCUMENT TYPE: Journal LANGUAGE: English
IT 124076-63-7
RL: BIOL (Biological study)

CODEN: EJPPET; ISSN: 0922-4106

DOUMENT TYPE: Journal

LANGUAGE: English

IT 124076-63-7 RL: BIOL (Biological study)

(MDDA receptor antagonism by, neurotoxicity and neuroprotective activity in relation to)

RN 124076-63-7 CAPIUS

CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldimino)bis- (9CI) (CA

ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

$$\begin{array}{c|c} & \text{NH} & \text{NH} \\ \parallel & \parallel & \parallel \\ \text{H}_2\text{N-C} & \text{NH-} \left(\text{CH}_2\right)_4 \text{-NH-} \end{array}$$

125880-83-3 CAPLUS Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis{3-nitro-(9CI)}

125880-84-4 CAPLUS
Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis(3-nitro- (9CI)(CA INDEX NAME)

125880-85-5 CAPLUS
Benzenecarboximidamide, 4,4'-(1,3-propanediyldimino)bis(3-amino- (9CI)(CA INDEX NAME)

125880-86-6 CAPLUS
Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI)(CA INDEX NAME)

125880-87-7 CAPLUS
Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis(3-amino- {9CI} (CA INDEX NAME)

125880-89-9 CAPLUS Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis(3-amino- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{NH2} \\ \text{NH} - \text{CH}_2 - \text{CH}_2 - \text{NH} \\ \text{NH} \\ \text{NH} \end{array}$$

ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN CN INDEX 125880-81-1 CAPLUS
Benzenecarboximidamide, 4,4'-{1,3-propanediyldiimino}bis- (9CI) (CA NAME)

125880-82-2 CAPLUS Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)

125880-83-3 CAPLUS
Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI)(CA INDEX NAME)

Benzenecarbox midamide, 4,4'-(1,5-pentanediyldimino)bis[3-nitro- (9CI) (CA INDEX NAME)

ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS
The DNA binding properties of a series of bisbenzamidines related to the clin. used antipneumocystis drug pentamidine (I) were studied. Changes

the thermal denaturation temp. of calf thymus DNA (.DELTA.Tm) showed that all the compds. have significant affinity for DNA. A comparison of .DELTA.Tms for the series with .DELTA.Tms of base-pair-specific DNA-binding compds. using homopolymers poly(dA).cntdot.poly(dT) and poly(dG-dC).cntdot.poly(dG-dC), indicated that the compds. show moderate specificity for AT base pairs. Lack of DNA helix extension, measured by viscometric titrn. with sonicated calf thymus DNA, indicated that the compds. do not bind to DNA by intercalation. Analogs of I with an odd

of methylenes connecting the benzamidine rings had a higher affinity for DNA and homopolymers than analogs with an even no. of methylenes. All of the compds. contg. an amidino group meta to the linking chain showed

polynucleotide affinity. These results suggest that the shape of the mols. Was important for DNA binding. Mol. modeling studies showed a correlation between the DNA binding and the radius of curvature of mol. mechanics models of the mols. Monosubstitution on the benzamidine rings or replacement of the amidino group with the cyclic imidazolino group had no infiluence on the DNA-binding affinity of the compds. Substitution of NH for the ether oxygen connecting group of I had no effect on the DNA binding or base-pair specificity. Methylation of either of the nitrogen atoms of the imidazolino group to provide an analog of I with N-methylimidazolino groups decreased DNA affinity considerably. GC vs AT base-pair specificity as measured by .DELTA.Tm does not correlate with

base-pair specificity as measured by .DELTA.Tm does not correlate with
the
radius of curvature. The exptl. and modeling results are consistent with
DNA minor-groove binding.
ACCESSION NUMBER:
1992:75694 CAPLUS
116:75694
TITLE: Structure and DNA binding activity of analogs of
1,5-bis(4-amidinophenoxy)pentane (pentamidine)
AUTHOR(S): Cory, Michael; Tidwell, Richard R.: Fairley, Terri A.
CORPORATE SOURCE: Div. Org. Chem. Burroughs Wellcome Co., Research
Triangle Park, NC, 27709, USA
SOURCE: JOURNAMAR; ISSN: 0022-2623
DOCUMENT TYPE: AUGUSTA STREED CAPTER SOURCE: SIGNIAN
LANGUAGE: Regist
17 124076-63-7 125880-81-1 12580-82-2
125880-83-3 125800-84-4 125800-89-9
125880-86-6 125800-87-7 12580-89-9
NALL BAC (Biological activity or effector, except adverse); BSU

RL: BAC (Biological activity or effector, except adverse); BSU

logical study, unclassified); BIOL (Biological study) (DNR-binding activity of) 124076-63-7 CAPLUS Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA CN INDEX NAME)

ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS

125880-85-5 CAPLUS Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

125880-86-6 CAPLUS Benzenecarboximidamide, 4,4'-{1,4-butanediyldiimino}bis{3-amino- (9CI) (CA INDEX NAME)

Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino-(9CI)(CA INDEX NAME)

125880-89-9 CAPLUS
Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI)(CA INDEX NAME)

L8 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

LB ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 12580-82-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)

RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro-(9CI)(CA INDEX NAME)

RN 125880-84-4 CAPLUS
CN Benzencearboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro-(9CI)(CA INDEX NAME)

RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-{1,4-butanediyldiimino}bis[3-amino-(9CI)(CA INDEX NAME)

L8 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS
AB 1,5-Di(4-amidinophenoxy) pentane (pentamidine) and 38 analogs of pentamidine were screened for in vitro against the enteric protozoan Giardia lamblia WB (ATCC 30957). All compds. were active against G. lamblia as measured by a [methyl-3H]thymidine incorporation assay. Antigiardial activity varied widely, with 50% inhibitory concus. (IC50s) ranging from 0.51 .+- 0.13 .mu.M (mean .+- std. deviation) for the most active compd. to over 100.0 .mu.M for the least active compds. The IC50 of the most potent antigiardial agent, 1,3-di(4-amidino-2-methoxyphenoxy) propane compared favorably with the IC50s of the compds. currently used to treat giardiasis, i.e., furazolidone (1.0 .+- 0.03 .mu.M), metronidazole (2.1 .+- 0.03 .mu.M), quinacrine Hol (0.03 .+- 0.02 .mu.M), and tinidazole (0.78 .+- 0.48 .mu.M). A mode of antigiardial activity for these compds. was suggested by the correlation obsd. between antigiardial activity and the binding of the compds. to calf thymus DNA and poly(dA).poly(dT).

ACCESSION NUMBER: 1991:554848 CAPLUS

DOCUMENT NUMBER: 1991:554848

TITLE: Structure-activity relationships of pentamidine analogs against Giardia lamblia and correlation of antigiardial activity of the compds. to see the structure activity with DNA-binding affinity analogs against Giardia lamblia and correlation of antigiardial activity of the second process of the second process

$$\begin{array}{c|c} & \text{NH} & & \text{NH} \\ \parallel & & \parallel & \\ \text{L} & \text{NH} - (\text{CH}_2)_5 - \text{NH} \end{array}$$

RN 125880-81-1 CAPLUS CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldimino)bis- (9CI) (CA INDEX NAME)

L8 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-{1,5-pentanediyldiimino}bis{3-amino-{9CI}(CA INDEX NAME)

RN 125880-89-9 CAPLUS
CN Benzenecarboximidanide, 4,4'-(1,2-ethanediyldimino)bis[3-amino- (9CI) (CA INDEX NAME)

AB The antiprotozoal compd. 1,5-di(4-amidinophenoxy)pentane (pentamidine) and and 36 of its analogs were screened for in vitro activity against L. mexicana amazonensis clone 669 C48 (MHON/BR/N3W2569) and D. falciparum clones W2 (Indochina III/CDC) and D6 (Sierra Leone I/CDC). Pentamidine and each of the analogs tested exhibited activity in vitro against L. mexicana amazonensis and P. falciparum. The pentamidine analogs were more effective against he P. falciparum clones than against L. mexicana amazonensis. P. falciparum clones than against L. mexicana amazonensis. P. falciparum as extremely susceptible to these compds., with 50% inhibitory concns. as low as 0.03 .mu.M. While none of the analogs exhibited marked improvement in antileishmanial activity compared with pentamidine, 12 of the pentamidine analogs showed activity approx. equal to or greater than that of the parent compd. From the promising activity exhibited by the pentamidine analogs in this in vitro study and their potential for reduced toxicity relative to the parent drug, pentamidine-related compds. hold promise as new agents for the treatment of protozoal infections.

ACCESSION NUMBER: 1990:S84205 CAPLUS
113:184205

STRUCTURE-ACTIVITY relationships of analogs of pentamidine against Plasmodium falciparum and Leishmania mexicana amazonensis

AUTHOR(S): Bell, Constance A.; Hall, James Edwin; Kyle, Dennis E.; Grogl, Max; Ohemeng, Kwasi A.; Allen, Margaret A.;

Tidwell, Richard R. Sch. Public Health, Univ. North Carolina, Chapel

NC, 27599, USA

SOURCE: Antimicrobial Agents and Chemotherapy (1990), 34(7), 1381-6

CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal English

English

1 124076-63-7 125880-81-1 125880-96-6

125880-83-3 125880-89-9

RL: BAC (Biological activity)

125880-87-7 125880-89-9
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); BIOL (Biological study)
(antiprotozoal activity of, against Plasmodium falciparum and
Leishmania mecicana amazonensis, structure in relation to)
RN 124076-63-7 CAPLUS Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA

NAME)

$$\begin{array}{c} \text{NH} \\ \text{H}_2\text{N-c} \\ \\ \\ \text{NH-(CH}_2) \\ \text{5-NH-} \end{array}$$

125880-81-1 CAPLUS
Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA

ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

125880-87-7 CAPLUS

Benzenecarboximidamide, 4,4'-{1,5-pentanediyldiimino}bis[3-amino- (9CI) (CA INDEX NAME)

NH- (CH2)5-N NH2

125880-89-9 CAPLUS

Benzenecarboximidamide, 4,4'-{1,2-ethanediyldiimino}bis{3-amino- (9CI) (CA INDEX NAME)

ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

125880-82-2 CAPLUS Benzenecarboximidamide, 4,4'-(1,4-butanediyldimino)bis- (9CI) (CA INDEX NAME)

125880-83-3 CAPLUS
Benzenecarboximidamide, 4,4'-{1,3-propanediyldimino}bis[3-nitro- (9CI)

125880-84-4 CAPLUS
Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

125880-86-6 CAPLUS Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS

A series of 33 analogs of 1,5-bis(4-amidinophenoxy)pentane (pentamidine) was synthesized for screening against a rat model of P. carinii pneumonia

monia.
Twenty-five of the compds. showed efficacy against P. carinii pneumonia when compared to a saline-treated control group. Two compds., butamidine (I) and 1,3-bis(4-amidino-2-methoxyphenoxy)propane (II), were more effective than pentamidine in treating P. carinii pneumonia in the rat model of infection. In addn. to their activity against P. carinii pneumonia, the compds. were also evaluated for antitrypsin activity, ability to inhibit thymidylate synthetase, affinity for DNA, and city.

Dieter; Ohemeng, Kwasi A.; Cory, Michael; Hall, James Edwin Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27599, USA Journal of Medicinal Chemistry (1990), 33(4), 1252-7 CODEN: JMCMAR; ISSN: 0022-2623 Journal CORPORATE SOURCE: SOURCE:

DOCUMENT TYPE: LANGUAGE:

English CASREACT 112:151252 OTHER SOURCE(S): IT 125880-66-28

R SOURCE(S): CASREACT 112:151252
125880-66-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) [preparation]
(prepn. and hydrogenation of)
125880-66-2 CAPLUS
Benzenecartboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro-, dihydrochloride (9CI) (CA INDEX NAME)

IT 109563-82-8P 125880-64-0P 125880-65-1P 125880-67-3P 125880-68-4P 125880-69-5P 125880-70-9P 125880-73-1P RI: SPN (Synthetic preparation); PREP (Preparation) (prepn. and Pneumocystis carinii pneumonia inhibition by and toxicity of)
RN 109563-82-8 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldimino)bis-, dihydrochloride (9CI) (CA INDEX NAME)

●2 HC1

125880-64-0 CAPLUS
Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis-, dihydrochloride
(9CI) (CA INDEX NAME)

●2 HC1

RN 125880-65-1 CAPLUS CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis-, dihydrochloride (9CI) (CA INDEX NAME)

ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

4 HCl

125880-70-8 CAPLUS
Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino-,tetrahydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{NH2} \\ & \text{NH-} \text{ (CH2) 5-NH-} \\ & \text{NH2} \\ & \text{NH} \end{array}$$

●4 HC1

125880-73-1 CAPLUS
Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino-,tetrahydrochloride (9CI) (CA INDEX NAME)

●4 HC1

124076-63-7 125880-81-1 125880-82-2
125880-83-3 125880-84-4 125880-85-5
125880-86-6 125880-87-7 125880-89-9
RL: BIOL (Biological study)
{Pneumocystis carinii pneumonia inhibition by and toxicity of}
124076-63-7 CAPLUS
Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA

L8 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

$$\begin{array}{c|c} & \text{NH} & \text{NH} \\ \parallel & \parallel & \parallel \\ \text{H}_2\text{N-C} & \text{NH-(CH}_2)} & \text{S-NH-} \end{array}$$

●2 HC1

125880-67-3 CAPLUS
Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis(3-nitro-,dihydrochloride (9CI) (CA INDEX NAME)

●2 HC1

125880-68-4 CAPLUS Benzenecarboximidamide, 4,4'-{1,3-propanediyldiimino}bis{3-amino-, tetrahydrochloride (9CI) (CA INDEX NAME)

$$\stackrel{\text{NH2}}{\underset{\text{NH}}{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH}}{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}{\underset{\text{NH2}}}} = \stackrel{\text{NH2}}{\underset{\text{NH2}}} = \stackrel{\text{NH2}}{\underset{\text{NH$$

●4 HC1

125880-69-5 CAPLUS
Benzenecarboximidanide, 4,4'-(1,4-butanediyldiimino)bis[3-amino-,tetrahydrochloride (9CI) (CA INDEX NAME)

ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN CN INDEX 125880-81-1 CAPLUS Benzenecarboximidamide, 4,4'-{1,3-propanediyldiimino}bis- (9CI) (CA NAME)

125880-82-2 CAPLUS Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)

125880-83-3 CAPLUS Benzenecarboximidamide, 4,4'-(1,3-propanediyldimino)bis(3-nitro- (9CI)(CA INDEX NAME)

125880-84-4 CAPLUS
Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis(3-nitro-(9CI)(CA INDEX NAME)

125880-85-5 CAPLUS Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

125880-86-6 CAPLUS
Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis(3-amino- (9CI)
(CA INDEX NAME)

125880-87-7 CAPLUS Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

125880-89-9 CAPLUS Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME) RN CN

ANSWER 16 OF 19 CAPLUS COPYRIGHT 2003 ACS
A MPLC method was developed for the detection and quantification of
pentamidine and pentamidine analogs of chemotherapeutic value in order to
measure their concn. in physiol. fluids. The compds. were extd. from
urine over octadecyl solid-phase exth. columns, followed by chromatog.
sepn. with an octadecyl reversed-phase column. For the mobile phase, a
gradient of 31.5-37.5% MeCN in water, with Na heptanesulfonate and
N(Me)4Cl as ion modifiers, was used. This method was used to reliably
detect levels as low as 341 ng/mL without concn. of the compds. during the

solid-phase extn. The assay was used to det. the effectiveness of several

solid-phase extn. columns for isolating the compds. of interest and to quantify the amt. of pentamidine and its analogs contained in the urine

dosed rats.

ACCESSION NUMBER 1990:87 CAPLUS DOCUMENT NUMBER:

TITLE: High-performance liquid chromatographic method for

quantification of several diamidine compounds with potential chemotherapeutic value Berger, Bradley J.; Hall, James Edwin; Tidwell, Richard R. Sch. Public Health, Univ. North Carolina, Chapel

AUTHOR (S):

CORPORATE SOURCE: Hill,

NC, 27599, USA Journal of Chromatography (1989), 494, 191-200 CODEN: JOCRAM: ISSN: 0021-9673 Journal English SOURCE:

DOCUMENT TYPE: LANGUAGE: 124076-63+7

1440/6-63-7

RE: ANT (Analyte); ANST (Analytical study)
(detn. of, in urine by HPLC)
124076-63-7 CAPLUS
Benzenecarboximidamide, 4,4'-{1,5-pentanediyldiimino}bis- (9CI) (CA NAME)

ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

ANSWER 17 OF 19 CAPLUS COPYRIGHT 2003 ACS Similarities and differences of trypsin (I) and plasma kallikrein (II)

AB similarities and differences of trypsin (I) and plasma kallikrein (II) are interpreted. Various amidines were tested for inhibition of II activity with N-.alpha.-tosyl-L-arginine Me ester (TAME) as substrate. Results with 150 amidines in vitro showed that aliphatic amidines were inactive. Some aromatic amidines, bis-amidines more than mono-amidines, had considerable inhibitory action. All amidines acted as competitive inhibitors. Substitution of the amidine group gave a loss of activity. Results are tabulated with structural formulas of 7 aromatic amidines inhibiting tabulated with structural formulas of 7 aromatic amidines inhibiting tabulated with structural formulas of 7 aromatic amidines inhibiting TAME hydrolysis by kallikrein, I, thrombin, and plasmin. Several amidines were tested against burns in guinea pigs and turpentine-induced edema in the pleural cavity of rats. The results varied with exptl. conditions, but some amidines had activity against the exptl. irritations. In general, the in vitro inhibitory activity of amidines was more specific than in vivo activity. Compol. I.C.I. 54, 394, had marked activity against kallikrein, trypsin, thrombin, and plasmin in vitro.

ACCLSSION NUMBER: 1971:120730 CAPLUS
DOCUMENT NUMBER: 74:120730

ITILE: Inhibition of guinea pig plasma kallikrein by amidines
AUTHOR(S): Davies, George Edward; Lowe, J. S.
CORPORATE SOURCE: Pharm. Div., Imp. Chem. Ind., Macclesfield/Cheshire, UK

Davies, George Edward; Lowe, J. S. Pharm. Div., Imp. Chem. Ind., Macclesfield/Cheshire, UK Advances in Experimental Medicine and Biology (1970), 8, 453-60 CODEN: AEMBAP; ISSN: 0065-2598 Journal English

SOURCE:

CODEN: AEMBAP; ISSN: 0065-2598

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 32152-41-3

RL: BIOL (Biological study)

(kallikreins inhibition by)

RN 32152-41-3 CAPLUS

CN Propanediamide, N,N'-bis[4-{aminoiminomethyl}phenyl]-, dihydrochloride

(9CI) (CA INDEX NAME)

ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS
For diagram(s), see printed CA Issue.

f. CA 55, 8344c. A series of 4,4'-diamidinodiphenylamines with
substituents in the C6H6 rings and (or) on the central smino group was
described. Most of the compds. were active against Trypenosom
rhodesiense, but the activity was less against T. congolense. The most
active compd. was 4,4'-diamidino-2-methoxydiphenylamine-2RCl, with a
therapeutic ratio of 7.5 against the latter organism. Treatment of
4-amino-3-methylbenzonitrile in C5H5N with BzCl gave 75%
N-benzoyl-4-cyano-2-methylaniline, m. 153. degree. (alc.).
N-Benzoyl-4-cyano-2-mitroaniline similarly obtained m. 144-6.degree.. A
mixt. of N-benzoyl-p-cyanoaniline (1 mole), 0.98 mole Pc15, and 4 moles
CC14 was refluxed and the solvent and Pc0C13 removed in vacuo. The
residual imidoyl chlorides, readily hydrolyzed by moisture, were not
further purified but condensed directly with various phydroxybenzonitriles by one of the following processes. (A)
p-Hydroxybenzonitrile (1.1 moles) was added to 1 mole NaOEt in alc., 1
mole benzimidoyl chloride (Ia) in EZO-CHC13 added, then 0.25 mole anhyd.
Na2CO3, the mixt. stirred 1-2 hrs. at 0.degree., then 3-4 hrs. at room
temp., left overnight, the solid collected, and recrystd. from alc. (B)
The Na salt of 1 mole p-hydroxybenzonitrile in dry C5H5N was mixed with
molten Ia, heated a few min. on the steam bath, HZO added, and the oily
ppt. crystd. and recrystd. (C) The p-hydroxybenzonitrile (I mole) and Ia
were melted together, 1.5 moles anhyd. NEt3 added, the mixt. refluxed 2
hrs., HZO and a slight excess AcOH added; the benzimidates generally

sepd.
as oils which soon crystd. The following
HC:CH.C(CN):CH.CR:CN:CPhOC:CR1.C
H:C(CN):CH.CR:CN:CPhOC:CR1.C
H:C(CN):CH:CR2 (I) were thus obtained (R, R1, R2, process, % yield, and m.p. given): H, Me, H, A, 63, 142.5.degree.: H, Me, H, B, 39,
136-8.degree.: H, Me, H, G, 76, 140-1.degree.: Me, H, H, A, 45,
104.5.degree.: Me, H, H, B, -, 102-4.degree.: Me, Me, H, A, 79,
125-9.degree.: Me, Me, H, B, 58, 123-6.degree.: Me, Me, H, C, 83,
125-7.degree.: H, Cl, H, 25, 135-6.degree.: Me, Cl, H, A, 36,
124.degree.: H, Cl, Cl, A, 24, 167-8.degree.: H, NO2, H, A, 47,
136.degree.: NO2, H, H, A, 78, 192.degree.; NO2, NO2, H, B, 96,
134-6.degree.: NO2, H, H, A, 78, 192.degree.; NO2, NO2, H, B, 96,
198.degree.: NOE, M, M, A, 78, 192.degree.: The rearrangement of I to
benzoyldiphenylamines (II) was carried out as follows except in 3 cases of

I $\{R=R2=H,\ R=NO2,\ R=NO2,\ R1=R2=H\}$ and $R=R1=NO2,\ R2=H\}$ I were dissolved in an equal wt. of Dowtherm and the soln. refluxed 1-2

II were isolated by addn. of Et20 and crystd. from alc. II (R1 = R2 = H,

= Me) was not characterized but was hydrolyzed directly to the corresponding diphenylamine. I $(R=R2=H,\ R1=N02)$ rearranged

smoothly
in refluxing anisole and even in refluxing C5H5N, tars being formed at
higher temps. Two I (R = NO2, R1 = R2 = H: R = R1 = NO2, R2 = H) were
unaffected at the lower temps. and decompd. at 200.degree.. The

unaffected at the rower comparison of the following II, HC:CH.C(CN):CH.CR:CRB2; CH.CH:C(CN).CH:CR2, were thus obtained (R, Rl, R2, % yield, and m.p. given): H, Me, H, 94, 165-7.degree.; Me, Me, H, 98, 159-60.degree.: H, Cl, H, 84, 170-2.degree.: Me, Cl, H, 80, 167-8.degree.: H, Cl, Cl, 54, 204-5.degree.: H, NO2, H, 99,

ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued) 4,4'-dicyano-2,N-dimethyldiphenylamine, m. 112.degree. (alc.). Refluxing 5 g. 2-amino-4,4'-dicyanodiphenylamine in 25 ml. 98-100% HCO2H 1.5 hrs. gave 5-cyano-1-(p-cyanophenyl)benzimidazole, m. 289.degree. (AcOH). 2-Amino-4,4'-dicyanodiphenylamine (12.5 g.), 50 ml. C5H5N, and 30 ml. Ac20

refluxed 0.5 hr. gave 12 g. 2-acetamido deriv., m. 238-40.degree. (decompn.), converted by refluxing 1.5-2.0 hrs. in 40 ml. Dowtherm into 8.4 g. 5-cyano-1-(p-cyanophenyl)-2-methylbenzimidazole, m. 233.degree. 5-Cyano-1-(p-cyanophenyl)-2-phenylbenzimidazole similarly prepd., m. 182.degree., solidified, and m. 199.degree. 2-Amino-4,4'-dicyanodiphenylamine (10 g.), 100 ml. alc., 5 ml. 7.5N isethionic acid,

dicyanodiphenylamine (10 g.), 100 ml. alc., 5 ml. 7.5N isethionic acid, ml. H2O, and 5 ml. concd. HCl treated at 10.degree. with 5 g. NaNO2 in 10 ml. H2O and 5 ml. alc. and kept 3 hrs. at room temp. gave 95% 5-cyano-1-(p-cyanophenyl)benzo-1,2,3-triazole, m. 284.degree. (dicxane). 4,4'-Dicyano-2-nitrodiphenylamine (1 g.), 2 ml. ClCO2Et, 1 g. K2CO3, and 10 ml. MeZCO refluxed 2 hrs. gave 0.8 g. 4,4'-dicyano-N-ethoxycarbonyl-2-nitrophenylamine, yellow crystals, m. 123-4.degree. (alc.). Similarly, 4,4'-dicyano-2-hydroxydiphenylamine gave 4,4'-dicyano-N-ethoxycarbonyl-2-ethoxycarbonyloxydiphenylamine, m. 131.5-2.5.degree. (alc.). If the reaction was carried out with an excess of dinitrile, the product was 6-cyano-3-(p-cyanophenyl)benzoxazolone (IV), m. 290.degree. IV was best prepd. by the following procedute. NaOM (1.46 g.) in a little H2O and sufficient alc. to make 24 ml. added to 13.8 g. of the diethoxycarbonyl compd. in 50 ml. dioxane and 50 ml. alc., left 2-3 hrs., concd. HCl d.

d, and the whole dild. with H2O gave 8.8 g. IV. The nitriles were converted into the amidines (V), through the imidates, by the usual Pinner procedure. V were often isolated as HCl salts. Some of the more sol. salts were not too easily crystd. In such cases the bases were isolated and converted into the acetates. The following diamidines, HC:CH. (H2NC (:NH) [C:H. CR:CNRIC:CR2.CH:CC-(:NH) NH2]. CH:CH, were thus prepd. (R, R1, R2, solvent, time in days, amidine salt, crystn. solvent,

yield, and m.p. given): Me, H, H, CHCl3, 4, 2HCl, H2O, 94, -; H, Me, H, CHCl3, 2, 2HCl, aq. alc. and Et2O, 63, 330.degree.; H, Et, H, alc., 1, 2HCl, aq. alc.-Et2O, 57, above 300.degree.; Cl, H, H, CHCl3, 3, 2HCl,

38, above 300.degree.; H, Ph, H, CHCl3-dioxane, 6, 2HCl, aq. Me2CO, 70, above 300.degree.; H, Bz, H, CHCl3, 12, 2HCl, aq. Me2CO, 31,

above 300.degree: H, Bz, H, CHCl3, 12, 2HCl, aq. Me2CO, 31, 280.degree.; Me, H, CHCl3, 7, 2HCl, aq. Me2CO-alc., 47, 285.degree.; H, Bu, H, CHCl3, 4, diacetate, aq. Me2CO, 63, 275-80.degree.; H, allyl, H, CHCl3, 5, diacetate, 120 or aq. Me2CO, 67, 271-3.degree.; H, Fr, H, CHCl3-EL2O, 1, 2HCl, aq. Me2CO, 78, 232-8.degree.; H, p-C6H4C(:NH)NH2, H, CHCl3-dioxane, 10, 3HCl, aq. Me2CO, 50, 370-5.degree.; NH2, H, M, alc., 6, 2HCl, H2O, 54, 310.degree.; H, (CH2)3, H, alc., 2, 4HCl, aq. Me2CO, 67, 300-10.degree.; H, p-C6H4NH2, H, alc., 6, diacetate, aq. Me2CO, 67, 169.degree.; Me, Bz, Cl, alc., 1, diacetate, AcOH, -, 225-30.degree.; Me, H, Cl, dioxane, 2, 2HCl, 182O, 70, blove 350.degree.; Cl, H, CH, CHCl3-EL2O, 6, diacetate, aq. Me2CO, 63, 265.degree.; Cl, H, Cl, CHCl3-EL2O, 6, 2HCl, aq. Me2CO, 64, 300-04.50.degree.; OMe, H, H, CHCl3, 3, 2HCl, aq. Me2CO, 64, 110-15.degree.; OH, H, H, dioxane-EL2O, 4, 2HCl, aq. Me2CO, 54,

338-40.degree.; OEt, H, H, CHCl3, 6, 2HCl, aq. Me2CO, 85, 115-17.degree.; OBu, H, H, CHCl3, 1, 2HCl, aq. Me2CO, 85, 133-4.degree.; OCH:CHMe, H, H, CHCl3, 3, 2HCl, aq. Me2CO, 79, 108-10.degree.; OPr, H, H, CHCl3, 2, 2HCl, aq. Me2CO, 78, 125-8.degree.; H, NO, H, CHCl3, -2 HCl, aq. Me2CO, 88, greater than 300.degree.; OMe, Me, H, CHCl3, 2, dipropionate, aq. Me2CO,

ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued) glycol, the mixt. refluxed a few min., and the product pptd. by H2O and recrystd. (AcOH). Compd. no. 6A was prepd. by hydrolysis of the corresponding II with K2CO3 in ethylene glycol-anisole conte, a little H2O. The product resisted purification but an almost theoretical yield

pure nitro compd. (no. 6B) was obtained as follows. 4,4'Dicyanodiphenylamine (40 g.) was ground with 200 ml. AcOH, 400 ml. concd.
HNO3 added, and after 25 min. H20 added to yield compd. no. 6B, crystd.
from anisole; no. 7 (931) was obtained by addh. of 45 g. reduced Fe to 24
g. 4,4'-dicyano-2-nitrodiphenylamine in 60 ml. refluxing HCONNe2 and 40
ml. AcOH, adding after 0.5 hr. 400 ml. hot H2O, filtering the mixt and
working up sep. the ppt. and the filtrate. Compds. nos. 12-15 were
i.

working up sep. the ppt. and the filtrate. Compds. nos. 12-15 were d.
by demethylation of 4,4'-dicyano-2-methoxydiphenylamine to give the OH deriv. At the required temp. 197-203.degree.) part of the mixt. stirred deriv. At the required temp. (197-203.degree.) part of the mixt. stirred with dil. alc., and the solid dissolved in HCONNE-dioxane. Any Meo compd. was pptd. by excess SN NaOH; acidification gave the 2-OH deriv. The other 2-alkoxy derivs. were obtained by alkylation of this with the appropriate halide and K2CO31 in refluxing Me2CO. The following III were thus obtained (no. R. R., 1 * yield, and m.p. given): (1), Me, H. 85, 222.degree.; (2), Cl. R. 60, 211.degree.; (3), Me, Me, 38, 199-200.degree.; (4), Me, Cl., 73, 198.degree.; (5), OMe, H, 86, 145-6.degree.; (7), NNZ, H, 83, 238-9.degree.; (8), NNAC, H, 75, 191.degree.; (7), NNZ, H, 83, 238-9.degree.; (8), NNAC, H, 75, 238-40.degree.; (11), Cl., Cl., 243-4.degree.; (13), OFT, H., 73, 135-6.degree.; (14), CCR2HCH2L, H, 70, 135-6.degree.; (13), OFT, H., 73, 135-6.degree.; (14), CCR2HCH2L, H, 70, 135-6.degree.; (15), Bu, H, 80, 114-15.degree. 1,3-Trimethylene bis(p-tolueneaulfonate) (861), m. 95-6.degree.; (12), brentamethylene bis(p-tolueneaulfonate) (863), m. 95-6.degree.; (16.), and 2-hydroxyethyl p-tolueneaulfonate, a sirup (phenylurethan m. 135-6.degree.), were prepd. by the Ag salt method. N-Alkyl derivs. were prepd. by treating 1 mole 4,4'-dieynodiphenylwahne with 1.2-1.5 moles requisite alkyl p-toluenesulfonate, 1 mole K2CO3, anisole, and a trace of Cu bronze under reflux, the H2O removed, and replaced by anisole, after refluxing 3-4

the solvent added, the mixt. filtered, the solvent removed, and the residue recrystd. from alc. N-Aryl-4,4'-dicyanodiphenylamines were

prepd.

by treatment of 1 mole 4,4'-dicyanodiphenylamine in the presence of K2CO3 and a trace of Cu bronze in refluxing PhNO2 4-6 hrs. with an excess of

PhI, (b) p-bromonitrobenzene, or (c) p-bromobenzonitrile. The products from (a) or (b) were isolated by addn. of CHCl3 and evapn. The solid

(c) was collected, washed, and the dried solid extd. with hot HCONNe2. 4,4'-Dicyano-N-(p-nitrophenyl)-diphenylamine (1.7 g.) in 15 ml. refluxing HCONNe2 and 2.5 ml. AcOH treated with reduced Fe gave 1.25 g. amine. The following N-substituted 4,4'-dicyanodiphenylamines were thus obtained (N-substituent, solvent for crystn., % yield, and m.p. given): Me, alc., 89, 153. degree: Ft. alc., 55, 122-3.degree: Pr. alc., 63, 96.degree: allyl, alc., 71, 111-12.degree: Bu, Et2O, 41, 80-1.degree: C6H13, alc., 60, 77.degree: (PL2)3, dioxane, 50, 211-12.degree: Ph, alc., 78, 190-1.degree: Ph. alc., 78, 190-1.degree: (P-NCO6H4, PNNO2, 80, 346.degree: P-H2NC6H4, -, 73, 275.degree:; P-NCC6H4, PNNO2, 80, 346.degree: 4,4'-Dicyano-2-methoxydiphenylamine (1 g.), 1 g. p-McGH4SO3Me, 0.8 g. K2CO3, a trace of Cu bronze, and 10 ml. anisole refluxed 3 hrs. gave 0.95 g. 4,4'-dicyano-2-methoxy-N-methyldiphenylamine, m. 189-50.degree. (alc.). 4,4'-Dicyano-2-methyldiphenylamine, m. 189-50.degree. (alc.).

ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued) 44, 193-201.degree.; OMe, NO, H, CHCl3, -, diacetate, aq. Me2CO, 69, 192-3.degree.; Me, NO, H, CHCl3, -, diacetate, aq. Me2CO, 93, 227-8.degree. Addn. of 5.5 g. NaNO3 in 15 ml. H2O to a cold soln. of 4,4'-diamidino-2-methoxydiphenylamine 2HCl in H2O pptd. the sparingly

4,4'-diamidino-2-methoxydiphenylamine 2HCl in HZO pptd. the sparingly

sol.

nitrite as a solid. 2N HCl (40 ml.) added during 5-10 min. and the ppt.
redissolved, the soln. kept l hr., 25 ml. 5N NaOH added, the nitrosoanine
base collected and treated with AcoH gave 8 g. of the diacetate. The
diimidoate was prepd. in CHCl3dioxane and 76i 5-amidino-1-(pamidinophenyl)benzimidazole-2HCl collected, m. 305.degree. (aq. Me2CO).
5-Amidino-1-(p-amidinophenyl)-2-methylbenzimidazole-2HCl (67%) (HZO) and
5-amidino-1-(p-amidinophenyl)-2-methylbenzimidazole-2HCl (67%) (HZO) and
5-Amidino-1-(p-amidinophenyl)-2-methylbenzimidazole-2HCl (67%) (HZO) and
5-amidino-1-(p-amidinophenyl)-2-methylbenzimidazole-2HCl (67%) (HZO) and
5-amidino-1-(p-amidinophenyl)-2-methylbenzimidazole-2HCl (78%) (Me2CO-dil.
HCL) were prepd. similarly.

ACCESSION NUMBER: 1961:87461 CAPLUS
DOCUMENT NUMBER: 55:87461
DOCUMENT TNUMBER: 55:87461
Search for chemotherapeutic amidines. XVIII.
Substituted 4,4'-diamidinodiphenylamines
AUTHOR(5): Easson, A. P. T.
CORPORATE SOURCE: May & Baker Ltd., Dagenham, UK
SOURCE: J. chem. Soc. (1961) 1029-37
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT 108531-36-1, Benzamidine, 4,4',4'',4'''(trimethylenedinitrilo)tetra-, tetrahydrochloride
(prepn. of)
RN 10851-36-1 CAPLUS
CN Benzamidine, 4,4',4'',4'''(trimethylenedinitrilo)tetra-, tetrahydrochloride (6CI) (CA INDEX NAME)

ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS cf. CA 55, 521e. The title compds. and the piperazine deriv., 1,4-bis(p-amidinophenyl))piperazine (1) were described. They had no significant trypanocidal activity. p-Aminobenzamidine-HCl (8.5 g.) in 50 ml. alc. and 2 ml. 40% HCMD refluxed 0.5 hr. gave 4.3 g. bis(p-amidinophenyl)piperazine (1) me. 236-8.degree. (MeOH-MeZCO). CuCN (6.8 g.) and 10 ml. C5M5N heated to 120-30.degree., 9.25 g. 1,2-bis(p-bromoanilino)ethane-2HCl, m. 236-8.degree. (MeOH-MeZCO). CuCN (6.8 g.) and 10 ml. C5M5N heated to 120-30.degree., 9.25 g. 1,2-bis(p-bromoanilino)ethane added, the temp. raised to 215-20.degree., the C5M5M distd., the melt stirred at 195-200.degree. 3 hrs., added to 20 g. KCN in 50 ml. HZO (the oil sepd. and hardened), the liquor poured off, the mass ground with 2N HCl to give 14.5 g. solid, this sublimed, and the yellow sublimate (300-10.degree./0.1 mm.) (0.45 g.) crystd. gave 0.33 g. 1,2-bis(p-cyanoanilino)ethane (II), m. 205-6.degree. (AcOM). p-Aminobenzonitrile (100 g.), 142 g. NaHCO3, 160 g. C2H4Br2, and 400 ml. EUCOH2CH2CNO refluxed 18 hrs., the mixt. cooled to 10.degree., the insol. material removed, the filtrate dild. with H2O, and the brown granular solid collected. p-Aminobenzonitrile (51 g.) was recovered from the mother liquors. The brown solid crystd. gave 18 g. product, sublimed to afford 9 g. II. The lat filtered product afforded 6.6 g. 1,4-bis(p-cyanophenyl)piperazine (III), yellow needles, m. 275-7.degree. (anisole). p-Aminobenzonitrile (5 g.), 4.25 g. anhyd. Na2CO3, and 7.1 g. C2H4Br2 refluxed 3 hrs. at 150-5.degree., cooled. filtered, and the solid crystd. gave 1.4 g. III. II (27.5 g.) in 650 ml. EtoCH2CH2CO3 at 0-5.degree. satd. with HCl. left 10 days and the mixt. treated with 390 ml. sstd. alc. NH3 at 55-60.degree. gave 7.5 g. 1,2-bis(p-andinoanilino) ethane-2HCl (1V), plates, m. 353.degree. (decompn.) IV (7.5 g.) in 600 ml. H20 treated at 10-15.degree. with 508 ANOH gave 6.4 g. product, which suspended in 80 ml. MeOH with methanesulfonic acid gave

1,2-bis(p-amidinoanilino)ethane di(methanesulfonate), m. 301-2

degree. (MeOH). III (8.4 g.) in 150 ml. EtOCH2CH2OH satd. at 0.5.degree. with HC1

gave I.2HCl. I.2HCl (6 g.) in 750 ml. H2O basified and the base treated with 20 ml. 2N isethionic acid gave 5.5 g. I disethionate, yellow needles, m. 328.degree. (decompn.) (MeOH). p-Aminobenzonitrile (12 g.)

in

100 ml. 2N HCl and 150 ml. H2O stirred 1 hr. with 12 ml. 1,1,3,3-tetraethoxypropane, the 15 g. solid washed, and a soln. in 300

ml.

ml.

964 aq. CSHSN treated with 300 ml. H2O gave ll g.

1-(p-cyanoanilino)-3-(p-cyanophenylimino)-1-propene, m. 227-9.degree... p-Aminobenzonitrile (11.8 g.), 5.2 ml. 1,3-dibromopropane, 8.4 g. NaHCO3, and 50 ml. EtOCH2CH2OH refluxed overnight gave 3 g. 1,3-bis(p-cyanoanilino)-propane (V), m. 159-61.degree. (aq. alc.). 1-[p-Cyanoanilino)-3-(p-cyanophenylimino)-1-propene (11 g.) in 700 ml. HCONMe2 hydrogenated at room temp. with 1.6 g. PtO2 1.5 hrs. gave 4.15 g. V. 1,3-Bis(p-cyanoanilino)propane (10 g.) in 200 ml. alc. satd. with HCl at 0-5.degree. and the diimidoester-2HCl which which

sepd. during 1 week (14.1 g.) dissolved in 100 ml. refluxing H2O and 30 ml. satd. NaCl gave 5.8 g. 1,3-bis(p-amidoanilino)propane-2HCl, yellow plates, m. 316-18.degree. (decompn.). Na glutaconic aldehyde-2H2O (1.55 g.) in 50 ml. H2O added at 80-90.degree. to 2.36 g. p-aminobenzonitrile

20 ml. 2N H2SO4 and 120 ml. H2O, the mixt. stirred a further 10 min., and filtered gave 2.5 g. 1-[p-cyanoanilino]-5-[p-cyanophenyllmino]-1,3-pentadiene, m. 140-4.degree. (decompn.), which (2.4 g.) in 100 ml.

reduced at 30-5.degree. over 0.24 g. PtO2, the ppt. filtered off, washed, and extd. with CHCl3 gave 1.8 g. brown solid, m. 160-70.degree..

ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued) to purify this product were unsuccessful. The aq. dimethylformamide filtrate gave 0.2 g. p-aminobenzonitrile. p-Aminobenzonitrile (94.4 g.), 97.6 g. hexamethylene dibromide, 67.2 g. NaHCO3, 400 ml. ECORIZCH2OH, and a crystal of iodine refluxed 24 hrs., the solvent evapd., the residual

cooled, stirred with 2 1. 2N HCl, extd. with CHCl3, and the solvent removed gave 16 g. 1,6-bis(p-cyanoanilino)hexane (VI), prismatic needles, m. 165-7.degree. (AcOH). Similarly, 15 g. VI in 180 ml. EtOCH2CH2OH

at 0-5.degree. with HCl gave the di-HCl salt, converted to 5.2 g.

1,6-bis(p-amidinoanilino)hexane diisethionate, prisms, m. 238-40.degree.

(HZO and MeOH).

ACCESSION NUMBER: 1961:43097 CAPLUS
DOCUMENT NUMBER: 55:43097
ORIGINAL REFERENCE NO.: 55:8346-i,8345a-b
TITLE: Search for chemother aputic amidines. XVII.

| 1,6-bis(p-amidinoanilino)hexane diisethionate, prisms, m. 238-40.
(HZO and MeoN).

ACCESSION NUMBER: 1961:43097 CAPLUS
ORGINAL REFERENCE NO.: 55:83446-1,8345a-b

TITLE: Search for chemocherapeutic amidines. XVII.

| Alpha...omega.-Bis(p-amidinoanilino)alkanes

AUTHOR(S): Berg. S. S.

CORPORATE SOURCE: Northern Polytechnic, London

SOURCE: J. Chem. Soc. (1960) 5172-6

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

Unavailable

(hydrochloride
(prepn. of)

RN 109563-82-8 CAPLUS

CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldimino)bis-,

dihydrochloride
(9CI) (CA INDEX NAME)

●2 HC1

=> fil reg COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST

88.69 416.12

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE

-12.37 -16.28

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STRUCTURE FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4 DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L9 STRUCTURE UPLOADED

=> d query

L9 STR

$$NH_2$$

Structure attributes must be viewed using STN Express query preparation.

=> s 19

SAMPLE SEARCH INITIATED 16:28:56 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 17 TO ITERATE

100.0% PROCESSED 17 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 93 TO 587
PROJECTED ANSWERS: 0 TO 0

L10 0 SEA SSS SAM L9

=> s 19 full

FULL SEARCH INITIATED 16:29:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 433 TO ITERATE

100.0% PROCESSED 433 ITERATIONS 3 ANSWERS

SEARCH TIME: 00.00.01

L11 3 SEA SSS FUL L9

=> fil caplus

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
148.15
564.27

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
ENTRY
SESSION
CA SUBSCRIBER PRICE

0.00 -16.28

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FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6 FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L12 5 L11

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L12 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS AB Polyamine or polyamine analog-amino acid conjugates (M) -N (E) - (B-A-B-NH) 4-E
                    (E) - (B-A-B-NA) 3-B-A-B-N(M)-E [M is an amino acid; A is a bond, (cyclo) alkyl, (cyclo) alkyl, (cyclo) alkyl, (cyclo) alkyl, (cyclo) alkyl, (cyclo) alkynyl, or alkynyl; E is M, (cyclo) alkyl, (cyclo) alkynyl, alkynyl, or cycloaryl], including salts or stereoisomers, were prepd. for use as antiviral
  agents.

An example is the polyamine glutamine conjugate SL-11165
[NH2CH(CH2CH2CONH2)CON(Et)(CH2CH2CH2CH2CH2NH)4Et.bul.5Hcl]. Thus,
[E]-EthH(CH2)4NHCH2CH:CHCH2NH(CH2)4NHEt was prepd. by a multi-step sequence starting from 4-bromobutamentirile, N-
(mesitylsulfonyl)ethanamine, and [E]-2-butene-1,4-diol.

ACCESSION NUMBER: 2002:888472 CAPLUS

DOCUMENT NUMBER: 137:384565
                                                                                        137:384565
Preparation of polyamine or polyamine analog-amino acid conjugates as antiviral agents
Frydman, Benjamin; Marton, Laurence J.; Valasinas, Aldonia L.; Reddy, Venodhar K.; Gutierrez, Jesus A.
Slil Biomedical Corporation, USA; Eli Lilly & Company
   TITLE:
    INVENTOR (S):
    PATENT ASSIGNEE(S):
                                                                                         PCT Int. Appl., 70 pp.
CODEN: PIXXD2
    SOURCE :
    DOCUMENT TYPE:
                                                                                         Patent
    LANGUAGE:
                                                                                         English
    FAMILY ACC. NUM. COUNT:
    PATENT INFORMATION:
                                                                                                                                                                                                              DATE
                    PATENT NO.
                                                                               KIND DATE
                                                                                                                                                       APPLICATION NO.
WO 2002091989 A2 20021121 WO 2001-US43887 20011108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, EG, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AW, AZ, BY, KG, KZ, MD, RU, TJ, TM RN: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NI, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NZ, SN, TD, TG PRIORITY APPLIN. INFO: US 2000-246804P P 20001108

OTHER SOURCE (S): MARPAT 137:384565

TI 304911-05-SP, SL 11137 304911-11-3P, SL 11134

304911-12-4P, SL 11136

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
                  (Uses)
(prepn. of polyamine or polyamine analog-amino acid conjugates as antiviral agents)
304911-05-5 CAPUS
Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(iminomethylene)]bis-,tetrahydrochloride (9CI) (CA INDEX NAME)
                 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS
Conjugates of polyamines analogs conjugated to at least one amino acid of formula M-N(E)-(B-A-B-NH)4-E or M-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [wherein
                   = independently an amino acid, esp. glutamine, asparagine, lysine, ornithine, arginine, histidine, or citrulline; A = independently a bond, (cyclo) alkyl, (cyclo) alkenyl, a lkynyl, or cycloaryl; B = independently a bond, alkyl, or alkenyl; E = independently H, (cyclo) alkyl, (cyclo) alkenyl, alkynyl, or cycloaryl; and salts or stereoisomers
 thereof)

were tested and claimed for pharmaceutical use as anticancer agents. For example, the polyamine glutamine conjugate SI-11165

(NHZCH(CHZCHZCHNHZ)CON(Et) (CHZCHZCHZCHZNH) 4Et.bul. 5HC.) exhibited ID50 values of >31.65, 4.1, and >31.25 against the DuPro, PC-3, and LnCap prostate cancer cell lines, resp. In addn., conformationally restricted polyamine analogs were prepd. Thus, (E)-EthN(CHZ)4MHCHZCH:CHCHZNH(CHZ)4MH

Et was prepd. in a multi-step sequence starting from 4-bromobutanenitrile, N-mesitylethanamine, and (E)-2-butene-1, 4-diol.

ACCESSION NUMBER: 2002:368258 CAPLUS

DCULMENT NUMBER: 136:368292

TITLE: Preparation of conformationally restricted polyamine analogs and use of polyamine amino acid conjugates as
                                                                                       136:386292
Preparation of conformationally restricted polyamine analogs and use of polyamine amino acid conjugates as anticancer agents
Frydman, Benjamin; Marton, Laurence J.; Valasinas, Aldonia L.; Reddy, Venodhar K.
Slil Biomedical Corporation, USA
PCT Int. Appl., 74 pp.
CODEN: PIXXD2
Parent
  INVENTOR (S):
   PATENT ASSIGNEE (S):
   SOURCE:
   DOCUMENT TYPE:
                                                                                        Patent
                                                                                        English
2
   FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                    PATENT NO.
                                                                             KIND DATE
                                                                                                                                                     APPLICATION NO. DATE
                                                                             A2
                                                                                                 20020516
20011108
                    WO 2002038105
                                                                                                                                                      WO 2001-US43585
                   polyamine amino acid conjugates as anticancer agents) 304911-05-5 CAPLUS
                   Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(iminomethylene)]bis-,
tetrahydrochloride (9CI) (CA INDEX NAME)
```

L12 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)

●4 HC1

304911-11-3 CAPLUS Benzenecarboximidamide, Benzenecarboximidamide, 4,4'-[1,5-pentanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

●4 HC1

304911-12-4 CAPLUS
Benzencarbox;midamide, 4,4'-[1,6-hexanediylbis(iminomethylene)]bis-,
tetrahydrochloride (9CI) (CA INDEX NAME)

●4 HC1

304911-12-4 CAPLUS Benzenecarboximidamide, 4,4'-[1,6-hexanediylbis(iminomethylene)]bis-,tetrahydrochloride (9C1) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ &$$

●4 HC1

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ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS Microsporidia are eukaryotic obligate intracellular protists that are emerging pathogens in immunocompromised hosts, such as patients with AIDS or patients who have undergone organ transplantation. We have demonstrated in vitro and in vivo that synthetic polyamine analogs are effective antimicrosporidial agents with a broad therapeutic window. CDB-knockout mice or nude mice infected with the microsporidian Encephalitozoon cuniculi were cured when they were treated with four different novel polyamine analogs at doses ranging from 1.25 to 5 mg/kg
     of
body wt./day for a total of 10 days. Cured animals demonstrated no
evidence of parasitemia by either PCR or histol. staining of tissues 30
days after untreated control animals died.
ACCESSION NUMBER: 2002:30291 CAPLUS
DOCUMENT NUMBER: 136:318859
Novel synthetic polyamines are effective in the
treatment of experimental microsporidiosis, an
opportunistic AIDS-associated infection
AUTHOR(S): Bacchi, Cyrus J.; Weiss, Louis M.; Lane, Schenells;
Frydman, Benjamin; Valasinas, Aldonia; Reddy,
Venodhar; Sun, Jerry S.; Marton, Laurence J.; Khan,
Imitiaz A.; Moretto, Magali; Yarlett, Nigel; Wittner,
Murray
                                                                                                                        Murray Murray Haskins Landon Departments of Biology and Chemistry, Pace University, New York, NY, 10038-1598, USA Antimicrobial Agenta and Chemotherapy (2002), 46(1),
       CORPORATE SOURCE:
   Antimicrobial Agents and Chemothe
55-61
CODEN: ANACCQ: ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANG JOSEPH TYPE: Langlish
THE PAC (Pharmacologies:
(Biologies: PAC (Pharmacologies: 1000)
                            30491-11-3, St 11134
Rt: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (USES)
(St 11134; novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)
304911-11-3 CAPLUS
Benzenecarboximidamide, 4,4'-{1,5-pentanediylbis(iminomethylene)}bis-, tetrahydrochloride (9CI) (CA INDEX NAME)
                                                                           CH2-NH-(CH2)5-NH-CH2
                                                                                                             ●4 HC1
                           304911-12-4, SL 11136
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SL 11136; novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. Infection) 304911-12-4 CAPLUS
                             Benzenecarboximidamide, 4,4'-[1,6-hexanediylbis(iminomethylene)]bis-,
                         ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
Novel conformationally restricted polyamines, such as E-NH-(B-A-B-NH)4-E
[A, E = bond, alkyl, alkenyl, alkynyl, cycloalkyl, cycloaryl,
cycloalkenyl: B = bond, alkyl, alkenyl), were prepd. for pharmaceutical
use as anticancer agents. Thus, (E)-EtNH(CH2)4NHCH2CH:CHCH2NH(CH2)4NHEt
was prepd. in a multistep sequence starting from mesityl chloride
4-bromobutanenitrile, N-mesitylethanamine, and (E)-2-butene-1,4-diol.
                             prepd. polyamines were tested for antiproliferative activity against
   human

Prostate cancer cell lines, such as PC3 and DUPRO.

ACCESSION NUMBER: 2000:790505 CAPLUS

DOCUMENT NUMBER: 133:35095

INVENTOR(S): Preparation of conformationally restricted polyamine analogs as disease therapies

INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Reddy, Venodhar K.; Valasinas, Aldonia; Blokhin, Andrei V.; Basu, Hirak S.

PATENT ASSIGNEE(S): Sill Blomedical Corporation, USA

POURCE: PIXED: PATENT LANGUAGE: PROLUMENT TYPE: Patent

LANGUAGE: PROLUMENT TYPE: Patent

LANGUAGE: PROLUMENT TYPE: Patent

English

FAMILY ACC. NUM. COUNT: 1
      FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
PATENT NO. . KIND DATE APPLICATION NO. DATE

WO 2000066587 A3 20001109 WO 2000-US11591 20000427
WO 2000066587 A3 20010125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, LD, LI, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LK, LT, LU, LV, MA, MD, MG, MK, MN, MW, MM, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RN: GH, GM, KE, LS, MM, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GM, ML, MR, NE, SN, TD, TG
EF 1177197 A2 200202016 EP 2000-928583 20000427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
BR 2000010701 A 20020213 BR 2000-10701 20000427
PRIORITY APPLM. INFO: : W02001-W11799 W 20000427

CTHER SOURCE(51)
                             PATENT NO.
                                                                                                        KIND DATE
                                                                                                                                                                                                         APPLICATION NO. DATE
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L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS tetrahydrochloride (9CI) (CA INDEX NAME) (Continued)

304911-05-5, SL 11137
RL: PRC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SL 11137; novel synthetic polyamines are effective in treatment of exptl. microsportidiosis, opportunistic AIDS-assocd. infection) 304911-05-5 CAPLUS
Benzenecarboximidamide, 4,4*-[1,4-butanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

●4 HC1

REFERENCE COUNT:

THERE ARE 45 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)

●4 BC1

304911-11-3 CAPLUS
Benzenecarboximidamide, 4,4'-[1,5-pentanediylbis(iminomethylene)]bis-,
tetrahydrochloride (9CI) (CA INDEX NAME)

●4 HC1

304911-12-4 CAPLUS
Benzenecarboximidamide, 4,4'-{1,6-hexanediylbis(iminomethylene)}bis-,
tetrahydrochloride (9CI) (CA INDEX NAME)

●4 HC1

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L12 ANSWER 5 OF 5 CAPLUS: COPYRIGHT 2003 ACS

AB The invention relates to peptide conjugates in which cytocidal and cytostatic agents, such as polyamine analogs or naphthoquinones, are conjugated to a polypeptide recognized and cleaved by enzymes such as prostate-specific antigen (PSA) and cathepsin B. Methods of using these conjugates in the treatment of prostate diseases are also provided.

Thus.
 Thus, C2[CH2NH(CH2) 4NHEt]2.4HC1 (SL-11103), 4-[[7-[4-(9-
acridinylamino)phenyl]heptyl]oxy]-1,2-naphthoquinone (SL-11064), and
morpholino-Ser-Lys-Leu-Gin-.beta.-Ala-.beta.-lapachone (SL-11147) were
prepd. and assayed for antitumor activity against human prostate cancer
cell lines, such as PC-3 and DUBRO.

ACCESSION NUMBER: 2000:790358 CAPLUS
DOCUMENT NUMBER: 133:350515

Freparation of novel polyamine analog conjugates and
quinone conjugates as therapies for cancers and
prostate diseases
INVENTOR(S): Frydman, Benjamin: Marton, Laurence J.
SOURCE: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Enclish
      DOCUMENT TYPE:
LANGUAGE:
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English
1
    FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT NO. KIND DATE

WO 2000066175 A2 20001109 WO 2000-US11542 20000427

WI AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, LV, HA, MD, MG, MK, MN, MW, KX, CA, CL, LK, LR, LS, LT, LU, LV, HA, MD, MG, MK, MN, MW, KX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TT, TZ, LA, GU, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, KW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, CG, CI, CM, GA, GN, MW, MM, KN, CN, NZ, PL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1173223 A2 20020123 EP 2000-928565 20000427

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

BR 2000010700 A 20020213 JP 2002-615058 20000427

PRIORITY APPLN. INFO: WARREN 12212424 W 20000427
                                                                                                                                                                                                                                                                         APPLICATION NO. DATE
```

BR 2000010700 A 20020213 BR 2000-10700 20000427

JP 2002543163 T2 20021217 JP 2000-615058 20000427

PRIORITY APPLN. INFO: US 1999-131809P P 19990430

WO 2000-US11542 W 20000427

OTHER SOURCE(S): MARPAT 133.350515

IT 30491-13-3P, SL 11134 304911-12-4P, SL 11136

RE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified): SDN (Suretains)

logical study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of novel polymaine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases) 304911-11-3 CAPLUS Benzenecarboximidamide, 4,4'-[1,5-pentanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

L12 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)

●4 HC1

304911-12-4 CAPLUS
Benzenecarboximidamide, 4,4'-[1,6-hexanediylbis(iminomethylene)]bis-,tetrahydrochloride (9CI) (CA INDEX NAME)

●4 HC1

30491-05-5P, SL 11137
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases)
304911-05-5 CAPLUS
Benzenecarboximidamide, 4,4'-{1,4-butanediylbis(iminomethylene)}bis-,.tetrahydrochloride (9CI) (CA INDEX NAME)

●4 HCl

=> fil reg

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 24.77 589.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
ENTRY
SESSION
CA SUBSCRIBER PRICE

-3.26
-19.54

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STRUCTURE FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4 DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09560711.str

L13 STRUCTURE UPLOADED

=> d query L13 STR

NH₂

Structure attributes must be viewed using STN Express query preparation.

=> s 113

SAMPLE SEARCH INITIATED 16:32:21 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 5 TO 234 PROJECTED ANSWERS: 0 TO 0

L14 0 SEA SSS SAM L13

=> s l13 full

FULL SEARCH INITIATED 16:32:25 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 56 TO ITERATE

100.0% PROCESSED 56 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

L15 0 SEA SSS FUL L13

=> Uploading 09560711.str

L16 STRUCTURE UPLOADED

=> d query

L16 STR

Structure attributes must be viewed using STN Express query preparation.

=> s 116

SAMPLE SEARCH INITIATED 16:33:25 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 21 TO ITERATE

100.0% PROCESSED 21 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS:

146 TO

PROJECTED ANSWERS:

0 TO 0

L17

0 SEA SSS SAM L16

=> s 116 full

FULL SEARCH INITIATED 16:33:30 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 465 TO ITERATE

100.0% PROCESSED 465 ITERATIONS 2 ANSWERS

SEARCH TIME: 00.00.01

L18 2 SEA SSS FUL L16

=> fil caplus

COST IN U.S. DOLLARS

SINCE FILE TOTAL

ENTRY SESSION 296.30

FULL ESTIMATED COST

885.34

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

CA SUBSCRIBER PRICE

ENTRY SESSION 0.00 -19.54

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FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6 FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 118

L19

1 L18

=> d l19 abs ibib hitstr

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
Arom dicationic compds., such as pentamidine, have potent antimicrobial
activities: Clin. use of these compds, has been restricted, however, by
their toxicity and limited oral activity. A novel approach, using
amidoxime derivs. as prodrugs, has recently been proposed to overcome
these limitations. Although results were presented for amidoxime derivs.
of only one diamidine, pentamidine, the authors in the original proposal
claimed that amidoxime derivs. would work as effective prodrugs for all
pharmacol. active diamidines. Nine novel amidoxime derivs. were
synthesized and tested in the present study for activity against
Pheumocystis carinii in corticosteroid-suppressed rats. Only three of

nine compds. had significant oral anti-Pneumocystis activity. The bisbenzamidoxime derivs. of three direct pentamidine analogs had

nine compos. nad significant oral anti-Pneumocystis activity. The bisbenzamidoxime derivs. of three direct pentamidine analogs had excellent oral and i.v. activities and reduced acute host toxicity. These compds. are not likely candidates for future drug development, however, because they have chronic toxic effects and the active amidine compds. have multiple sites susceptible to oxidative metab., which complicates their pharmacol. and toxicol. Novel diamidoximes from three other structural classes, contg. different groups linking the cationic moleties, lacked significant oral or i.v. anti-Pneumocystis activity, even though the corresponding diamidines were very active i.v. Both active and inactive amidoximes were readily metabolized to the corresponding damidines by cell-free liver homogenates. Thus, the amidoxime prodrug approach may pharmacol. activities of selected, but certainly not all, arom. diamidines.

ACCESSION NUMBER: 1998:189774 CAPLUS
DOCUMENT NUMBER: 128:303628
TITLE: Anti-Pneumocystis activities of aromatic diamidoxime prodrugs

1998:189774 CAPLUS
128:303628
Anti-Pneumocystis activities of aromatic diamidoxime prodrugs
Hall, James Edwin; Kerrigan, John E.; Ramachandran, Kishore; Bender, Brendan C.; Stanko, Jason P.; Jones, Susan K.; Patrick, Donald A.; Tidwell, Richard R. Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, Kc, 27599, USA Antimicrobial Agents and Chemotherapy (1998), 42(3), 666-674
CODEN: ANACCQ; ISSN: 0066-4804
American Society for Microbiology
Journal
English

CODEN: AMACCQ: ISSN: 0066-4804

American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

T 206532-31-2F

RI: BAC (Biological activity or effector, except adverse): BPR

(Biological process): BSU (Biological study, unclassified): PRF (Properties): SPN (Synthetic preparation): TMU (Therapeutic use): BIOL (Biological study): PREP (Preparation): PROC (Process): USES (Uses)

(anti-Fneumocystis activities of arom. diamidoxime prodrugs in relation

(anti-Pneumocystis activities of arom. diamidoxime prodrugs in relation
to structure and metab. and toxicity)
RN 206532-31-2 CAPIUS
CN Benzamide, N,N'-1,2-ethanediylbis[4-[{hydroxyamino}iminomethyl]- {9CI} (CA INDEX NAME)

L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS (Continued)

IT 206532-32-3P
RJ: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(anti-Pneumocystis activities of arom. diamidoxime prodrugs in

relation

to structure and metab. and toxicity)

RN 206532-32-3 CAPLUS

CN Benzamide, N,N'-1,2-ethanediylbis[4-(aminoiminomethyl)- (9CI) (CA INDEX NAME)

=> fil reg

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 5.79 891.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE -0.65 -20.19

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TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

""
Uploading 09560711.str

L20 STRUCTURE UPLOADED

=> d query

L20 STR

$$NH_2$$

$$NH_2$$

$$NH_2$$

$$NH_2$$

$$NH_2$$

Structure attributes must be viewed using STN Express query preparation.

=> s 120

SAMPLE SEARCH INITIATED 16:39:51 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 3553 TO ITERATE

28.1% PROCESSED 1000 ITERATIONS INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED) SEARCH TIME: 00.00.01

0 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**
PROJECTED ITERATIONS: 67487 TO 74633

PROJECTED ANSWERS:

0 TO

0

L21

0 SEA SSS SAM L20

=> s 120 full

FULL SEARCH INITIATED 16:40:01 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 72286 TO ITERATE

100.0% PROCESSED 72286 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.02

L22

0 SEA SSS FUL L20

=>

Uploading 09560711.str

L23 STRUCTURE UPLOADED

=> d queyr

L23 HAS NO ANSWERS

'QUEYR ' IS NOT A VALID STRUCTURE FORMAT KEYWORD

Structure Formats

SIA ---- Structure Image, Attributes, and map table if it contains data. (Default)

SIM ---- Structure IMage.

SAT ---- Structure ATtributes and map table if it contains data.

SCT ---- Structure Connection Table and map table if it contains

data.

SDA ---- All Structure DAta (image, attributes, connection table and map table if it contains data).

NOS ---- NO Structure data.

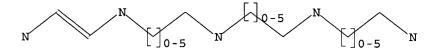
ENTER STRUCTURE FORMAT (SIM), NOS:nos

L23 STR

=> d query

L23

STR



Structure attributes must be viewed using STN Express query preparation.

=> s 123

SAMPLE SEARCH INITIATED 16:41:20 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 3553 TO ITERATE

28.1% PROCESSED 1000 ITERATIONS INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 67487 TO 74633 PROJECTED ANSWERS: 0 TO 0

L24

=> s 23 full L25 460971 23

=> s 123

SAMPLE SEARCH INITIATED 16:41:46 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 3553 TO ITERATE

28.1% PROCESSED 1000 ITERATIONS INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED) SEARCH TIME: 00.00.01 0 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS:

67487 TO 74633

PROJECTED ANSWERS:

0 TO

L26

0 SEA SSS SAM L23

=> s 123 full

FULL SEARCH INITIATED 16:41:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 72286 TO ITERATE

100.0% PROCESSED 72286 ITERATIONS

6 ANSWERS

SEARCH TIME: 00.00.01

L27 6 SEA SSS FUL L23

=> fil caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 304.12 1195.25 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL SESSION ENTRY CA SUBSCRIBER PRICE 0.00 -20.19

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FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6 FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 127 L28 3 L27

=> d 128 1-3 abs ibib hitstr

ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
The possibility of electron binding by a mol. with two polar ends, each L28 which is capable of electron binding, is studied using electronic structure methods. The destabilizing effects of each dipole on the ability of the other dipole to bind an electron as well as the through-bond splitting between the g and u anion states are examd. In addn., the ability of the two polar ends to bind two electrons, one to each end, is investigated. Numerical results are presented for the anions of (HCN)n .cntdot..cntdot..cntdot. HCCH .cntdot..cntdot..cntdot. (NCH)n (n = 2-4) and for the corresponding n = 2 dianion.

ACCESSION NUMBER: 2000:508846 CAPLUS
DOCUMENT NUMBER: 133:286775
TITLE: Bi-dipole-bound anions
AUTHOR(s): Gutowski, M., Skurski, P.; Simons, J.
CORPORATE SOURCE: Materials Resources, Pacific Northwest National
Laboratory, Richland, WA, 99352, USA
SOURCE: International Journal of Mass Spectrometry (2000), 201(1-3), 245-252
CODEN: IMSPF8; ISSN: 1387-3806
DOCUMENT TYPE: Journal PUBLISHER: DOCUMENT TYPE: LANGUAGE: IT 300347-22-2 IT 30347-22-2
RL: PRP (Properties)
(electronic structure and electron attachment ene
RN 300347-22-2 CAPFUS
Methanimidamide,
N',N'''-1,2-ethenediylbis[N-[[[(methyleneamino)methylene]
amino)methylene]- (9CI) (CA INDEX NAME) cture and electron attachment energy of)

PAGE 1-A

PAGE 1-B

PAGE 1-B

= CH2

THERE ARE 30 CITED REFERENCES AVAILABLE FOR RECORD. ALL CITATIONS AVAILABLE IN THE RE

L28 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS (Continued)

REFERENCE COUNT:

29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR

FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE RE

ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

AB Treatment of peptides contg. an .alpha.-(chloro)glycine residue with triethylamine and catalytic amts. of triphenylphosphine constitutes an efficient method for the stereoselective synthesis of amino acid and peptide dimers bridged by a C=C double bond. The dimers can be converted into novel peptide structures by std. methods of peptide synthesis.

ACCESSION NUMBER: 2000:447433 CAPLUS

DOCUMENT NUMBER: 133:208164

TITLE: Stereocontrolled backbone connection of peptides by C=C-double bonds

AUTHOR(S): Schumann, Susanne: Zeitler, Kirsten; Jager, Martin; Pollorn, Kurt: Steplich, Wolfgang

CORPORATE SOURCE: Department Chemie der Ludwig-Maximilians-Universitat Munchen, Munchen, D=0137, Germany

SOURCE: TetraBa [158N: 0040-4020

FUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 133:208164 290346-38-2P RL: SPN (Synthetic preparation); PREP (Preparation) (stereocontrolled prepn. of a triple dimeric peptide linked via C=C (stereocontrolled prepn. of a triple dimeric peptide linked via C=C double bonds) 290346-38-2 CAPLUS Aspartic acid, (ZE)-2,3-didehydro-N-[(1,1-dimethylethoxy)carbonyl]-3-[(1,1-dimethylethoxy)carbonyl]amino]aspartoylbis[q]ycyl-L-valyl-2,3-didehydro-3-[([(ZS)-1-([phenylmethoxy)carbonyl]-2-pyrrolidinyl]carbonyl]amino]-, tetramethyl ester, [4(2Z),4'(2Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS RWWINHCHR2CHR3CH2COR1 [I; R = H, acyl, (protected) Pro, pyroglutamyl; W = Phe, His, Leu, Tyr, 1-naphthylalanyl; W1 = Phe, His, Leu, Tyr, Nle: the N of the WW1 peptide link may be substituted by C1-4 alkyl when W = Phe and W1 = His; R2 = H, C1-6 alkyl, Ph, C4-7 cycloalkyl, C7-9 phenylalkyl, Occoloalkyl (alkylene); R3 = OH, amino, acylamino, alkoxy, alkoxycarbonyl; R1 = amino, C1-4 alkoxy, 4-benzylpiperazin-1-yl, 1,2,3,4-tetrahydroquinolin-1-yl, A-E-B, etc.; A = Lys, Pro, Ile; E = Phe, Gly, Ala, Val, Ile, Lys, Orn, Arg, Asp, etc.; B = OH, alkoxy, amino, glutamyl, etc.] and their salts were prepd. as renin inhibitors.

BOC-Phe-His-Sta-Ile-Sta-OR (Sta = 4S-amino-33-hydroxy-6-methylheptanoyl), prepd. by the soln. phase method, inhibited renin with an IC50 of <4.

.mu.mol/L. C5-10

ACCESSION NUMBER: 1989:173764 CAPLUS DOCUMENT NUMBER:

TITLE: Preparation and testing of statine-containing peptides

as renin inhibitors

Bindra, Jasit S.; Kleinman, Edward F.; Rosati, Robert INVENTOR(S):

PATENT ASSIGNEE(S):

L. Pfizer Inc., USA
U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 763,768, abandoned. SOURCE :

CODEN: USXXAM Patent English 2 DOCUMENT TYPE: LANGUAGE:

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE US 1986-839010 CA 1985-476191 US 1984-588279 CA 1985-476191 US 1985-763768 US 4749687 CA 1254699 A Al 19880607 19860310 19850311 19840312 PRIORITY APPLN INFO :

OTHER SOURCE(S): IT 118384-89-7P MARPAT 110:173764

RE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and hydrogenolysis of, in prepn. of renin inhibitor) 118384-89-7 CAPLUS

Lefistidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[2-hydroxy-4-{[2-methyl-1-[[[2-oxo-2-(phenylmethoxy)-1-

(phenylmethyl)ethyl][(phenylmethoxy)carbonyl]amino]methylene]butyl]amino]
1-(2-methylpropyl)-4-oxobutyl]-, (IS-[IR*,2R*,4[R*(R*)]]]- (9CI) (CINDEX NAME)

с сн₂- Рh Ph- CH2- CH-С-ин о 1-ви он -o-cH2-Ph L28 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS (Continued)

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn of, as intermediate for renin inhibitor)

II 118403-86-87 118403-87-87-87
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study; PREP (Preparation) (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. of, as renin inhibitor)

RN 118403-86-4 CAPLUS
CL L-Histidinamide,
N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-[[1-

{[(1-carboxy-2-phenylethyl)amino]methylene]-2-methylbutyl]amino]-2-hydroxy1-(2-methylpropyl)-4-oxobutyl]-, [1S-[1R*,2R*,4[R*(R*)]]]-, monoacetate
(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 118403-85-3 CMF C43 H61 N7 O8

CM 2

CRN 64-19-7 CMF C2 H4 O2

L28 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS (Continued)

=> fil reg

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
14.03
1209.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL
ENTRY SESSION
CA SUBSCRIBER PRICE

-1.95
-22.14

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STRUCTURE FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4 DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> fil caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 2.00 1211.28 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE 0.00 -22.14

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FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6 FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

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=> s polyamine

28502 POLYAMINE

29335 POLYAMINES

L29 40432 POLYAMINE

(POLYAMINE OR POLYAMINES)

=> s conformation?

L30 294106 CONFORMATION?

=> s 129 and 130

L31 672 L29 AND L30

=> logoff y

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 4.28 1215.56

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE 0.00 -22.14

STN INTERNATIONAL LOGOFF AT 16:46:58 ON 06 FEB 2003